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ORIGINAL ARTICLE

Risk factors for incident symptomatic knee osteoarthritis: A population-based case control study in Lebanon

Nabil EL AYOUBI,[1] Monique CHAAYA,[2] Ziyad MAHFOUD,[3] Rima R. HABIB,[4] Imad UTHMAN[1] and Zeinab N. SLIM[2]

[1]*Department of Internal Medicine,* [2]*Department of Epidemiology & Population Health American University of Beirut, Beirut, Lebanon,* [3]*Department of Public Health Weill Cornell Medical College-Doha, Doha, Qatar; and* [4]*Department of Environmental Health American University of Beirut, Beirut, Lebanon*

Abstract

Objectives: To identify risk factors for symptomatic knee osteoarthritis (OA) and explain the geographical disparities in its occurrence.

Methods: A population-based case control study used data from a national Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) study conducted in Lebanon in 2009. The sample included 59 incident cases of symptomatic knee OA with no past knee injury, knee pain for a period of < 12 months, and were examined by rheumatologists. One hundred and eighteen randomly sampled population-based controls were frequency matched with cases by age and gender.

Results: Obesity, overweight and area of residence were significant risk factors for knee OA, after adjusting for type of job, monthly income and family history of joint problems.

Conclusion: Determinants of symptomatic knee OA in Lebanon may differ by geographical location, potentially reflecting differences in social conditions, biological elements and environmental factors. The geographical differences remained significant even after accounting for investigated factors. Thus, further research is needed to explore other potential determinants, such as living conditions, biomechanical and hormonal factors.

Key words: epidemiology, osteoarthritis.

INTRODUCTION

Knee osteoarthritis (OA) is one of the most frequent types of arthritis, and its prevalence is expected to increase in the future.[1] The annual incidence of knee OA is around 0.01%, with a prevalence ranging between 1.4% and 19.3% worldwide.[2] In the Middle East, the prevalence of OA (including knee and hip) in Saudi Arabia[3] and Kuwait[4] is around 5%, which is similar to that in Lebanon, according to a recently published national Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) study from 2009.[5] However, a higher prevalence (16%) is reported in Egypt.[6] Knee OA is the main cause of difficulties in walking and climbing stairs as well as of knee replacement surgery.[1] It is also an important cause of lost time of leisure and work as well as early retirement.[7,8]

Several risk factors have been reported in the literature as potential risk factors for knee OA. Ageing is one well-defined risk factor for knee OA, with a prevalence increasing from 2- to near 10-fold in people between 30 and 60 years of age, and higher increases in persons above the age of 60.[9,10] As for gender, knee OA is more common among men below the age of 50, while it is more frequent among women above this age.[1] Other described risk factors of knee OA are

Correspondence: Prof Monique Chaaya, Department of Epidemiology and Population Health, American University of Beirut, 205A VanDyck Building, PO Box 11–0236, Riad El-Solh St., Beirut 1107–202, Lebanon.
Email: mchaaya@aub.edu.lb

obesity and overweight, classically related to OA due to mechanical overload of the knee joints,[1,11–15] but later related to OA by other potential biological mechanisms.[16–18] Occupations requiring repetitive weight-lifting and squatting[19] as well as repetitive knee torsion[13] and knee bending[14,20] have been associated with knee OA. Similarly, some types of sports involving repetitive intense knee torsion have been related to the disease.[21,22] Another associated factor studied was geographical location. A cross-sectional study in China showed that the prevalence of knee OA was significantly higher in northern than southern areas.[23] Other researchers explored the occurrence of joint replacement surgery due to knee OA in urban and rural areas of the USA, reporting a significantly higher occurrence of the disease in rural as compared to urban areas.[24] In both studies, the authors acknowledged the need for further studies to explain the differences in the distributions of the disease. Elements such as the physical environment or social practices could be determinants in shaping the differences among geographic areas.

In Lebanon, the national COPCORD on which the data of the current paper is built, which looked at the burden of various musculoskeletal conditions in the country, revealed important geographical variations in the distribution of knee OA, suggesting differences in the exposure to risk factors among Lebanese communities.[5] The present case-control study was carried out to identify risk factors for symptomatic knee OA in a Lebanese population, and to explain geographical disparities in its occurrence.

MATERIALS AND METHODS

This study is a secondary analysis of data from the national COPCORD "Community Oriented Program for Control of Rheumatic Diseases" study conducted in Lebanon in 2009, approved by the Institutional Review Board of the American University of Beirut. Using a multistage probability sampling of households, the COPCORD study explored the prevalence of rheumatic disorders in this country. Trained interviewers made a first visit to the sampled households and administered the COPCORD core questionnaire to a randomly selected member of the household who were 15 years of age and older. Further details are described elsewhere.[5] Participants who answered positively to the following question: "Have you suffered from pain/swelling/stiffness in the joints or musculoskeletal soft tissues within the last 7 days, or sometime in the past with pain intensity on the visual analogue scale $\geq$ 4" were examined in a second visit by Fellows in rheumatology. The American College of Rheumatology (ACR) criteria were used by the rheumatologists to report and classify OA.[25] When pertinent laboratory tests were indicated, a third visit was performed along with a trained registered nurse to obtain blood samples.

Selection of cases and controls

One hundred and twelve cases of knee OA were confirmed in the four governorates (Bekaa, North, Mount Lebanon and Beirut) (Fig. 1). From these, 59 were considered incident cases because they reported knee pain of < 12 months (mean = 2.5 months), did not present any type of arthritis in the past, and had no joint deformity at examination. The 12 months period is considered short enough to define incident cases, because the pain produced by knee OA starts insidiously,[26] being less likely to affect exposures among cases at the beginning of the disease. Furthermore, cases were identified clinically and not radiologically. This is considered adequate as the literature shows 88% sensitivity and 92% specificity of the clinical ACR criteria for knee OA among symptomatic patients.[26,27] Furthermore, radiological studies are used clinically to monitor the progression of knee OA or to rule out other disorders, rather than to identify new cases.[28] Nevertheless, radiological and laboratory assessments were done for five of the cases considered in this study to further confirm the diagnosis of knee OA.

Two population-based controls per case (118 controls) were selected randomly from the data (Fig. 1), frequency matched with the cases by 5-year-range age group and gender. Controls were participants who had never reported musculoskeletal problems. Since the negative predictive value of pain for even "early radiological" knee OA was described at around 88.4%,[27] it was reasonable to assume that individuals not reporting ever having knee pain would be most likely free of "symptomatic" knee OA. The number of prevalent cases (total = 112) found by governorate was the following: 60 in North Lebanon (8.1%), 31 in Bekaa (6.8%), 18 in Mount Lebanon (1.2%), and three in Beirut (0.8%). From these prevalent cases, the following were incident cases (total = 59) by governorate: 38 in North Lebanon, 15 in Bekaa, five in Mount Lebanon and one in Beirut. The final sample analyzed for this study included 177 participants (59 incident cases, 118 controls).

Measures

The domains explored in this case-control study were geographical (governorate, altitude), socio-economical

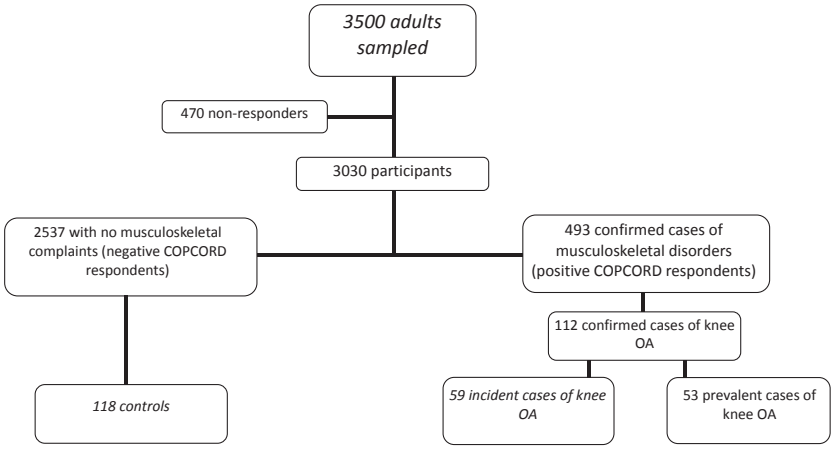

Figure 1 Flowchart showing the selection process of cases and controls based on the national Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) study in Lebanon, 2009.

(income, education), biological/constitutional (body mass index [BMI]), behavioral (cigarette smoking, type of leisure physical activity), familial predisposition (family history of joint problems) and occupational (type of job, type of repetitive movements at work).

The variables explored were: place of residence (North, Bekaa, Beirut/Mount Lebanon governorates); altitude above sea level (meters); household monthly income (low as < US$500, middle as US$500–2000 and high as > US$2000); level of education (low as elementary or below, medium as intermediate or high school, and high as university or technical); BMI (normal as < 24.9 kg/m^2, overweight as 25–29.9 kg/m^2 and obese as $\geq$ 30 kg/m^2); cigarette-smoking status (non smoker, ex-smoker and current smoker) and number of cigarettes per day; type of leisure physical activity (low impact as walking and swimming, or high impact as weight-lifting and soccer); presence of a family member with joint problems; type of present or past job (administrative, manual and agricultural or military); and type of repetitive movements at work (low impact as walking and standing, and high impact as kneeling, weight-lifting, and squatting). Regarding the variable type of present or past job, the categories agricultural and military were analyzed together since the nature of physical strain in both was shown to be much higher than in the manual types of jobs.

Regarding confounding factors, previous knee injury has been classically considered a confounder,[1] but in the 2009 COPCORD study, post-traumatic knee OA cases were not included, as in the present case-control study. Similarly, an interaction is described in the literature between obesity and previous knee injury, knee surgery, or Heberden's nodes,[1] but in the present study, none of the cases had these clinical features.

Statistical methods

With the exception of age and sex (the matching variables), all other variables were summarized for each of the two groups (cases and controls) using frequency distributions. Differences in such variables between the two groups were examined using the chi-squared distribution or Fisher's exact test (when cell counts were small). Variables with *P*-value $\leq$ 0.20 at the bivariate level were considered for inclusion in the multivariate logistic regression model. The final model included only variables from the latter group that either showed statistical significance or possible confounding effect. Both crude and adjusted odds ratios (OR), their corresponding 95% confidence intervals (95% CI) and two-sided *P*-values were reported. Significance was set at the 5% level. Log-likelihood ratio was used to assess the goodness of fit of the model. Analyses were performed using the Statistical Package for Social Sciences Version 16 (SPSS Inc., Chicago, IL, USA) and STATA Version 10 (STATACORP, College Station, TX, USA) software.

RESULTS

As shown in Table 1, the study sample comprised a higher proportion of females (56%), and a majority (57.6%) belonging to the age group between 45 and 64 years. The bivariate shows that residing in Bekaa and North, living in higher areas above sea level, low monthly income, low educational level, former cigarette smoking, positive family history for joint diseases, and being obese or overweight were all significantly associated with increased occurrence of knee OA. Considering occupational variables, participants with agricultural or military type of jobs had significantly higher odds of knee OA than those with administrative jobs. Similarly,

Table 1 Frequency distributions and bivariate associations of the study variables among cases and controls: Lebanon, 2009

Variable	Cases *n* (%)	Controls *n* (%)	Total *n* (%)	OR (95% CI)	*P*-value
Age group					
< 44 years	15 (25.4)	30 (25.4)	45 (25.4)	1	–
45–64 years	34 (57.6)	68 (57.6)	102 (57.6)	1.0 (0.5–2.1)	1.000
≥ 65 years	10 (16.9)	20 (16.9)	30 (16.9)	1.0 (0.4–2.7)	1.000
Sex					
Male	26 (44.1)	52 (44.1)	78 (44.1)	1	–
Female	33 (55.9)	66 (55.9)	99 (55.9)	1.0 (0.5–1.9)	1.000
Governorate					
Beirut/Mt Lebanon	6 (10.2)	81 (68.6)	87 (49.2)	1	–
Bekaa	15 (25.4)	9 (7.6)	24 (13.6)	22.5 (7, 72.6)	< 0.001*
North Lebanon	38 (64.4)	28 (23.7)	66 (37.3)	18.3 (7, 48)	< 0.001*
Body mass index (BMI)					
Normal (≤ 24.9 kg/m^2)	8 (13.6)	59 (50)	67 (37.9)	1	–
Overweight (25–29.9 kg/m^2)	19 (32.2)	40 (33.9)	59 (33.3)	3.5 (1.4, 8.8)	0.007*
Obese (≥ 30 kg/m^2)	32 (54.2)	19 (16.1)	51 (28.8)	12.4 (4.9, 31.5)	< 0.001*
Type of job					
Administrative (Office work, teaching)	16 (47.1)	47 (63.5)	63 (58.3)	1	–
Manual jobs (carpenter, worker in a restaurant or in small shop)	10 (29.4)	23 (31.1)	33 (30.6)	1.3 (0.5, 3.3)	0.608
Agriculture/military	8 (23.5)	4 (5.4)	12 (11.1)	5.9 (1.6, 22)	0.009*
Repetitive movements at work					
Never worked	29 (49.2)	50 (42.4)	79 (44.6)	1	–
Moderate knee impact (standing, walking)	24 (40.6)	67 (56.8)	91 (51.4)	0.6 (0.3, 1.2)	0.148
High knee impact (kneeling, squatting)	6 (10.2)	1 (0.8)	7 (4.0)	10.3 (1.2, 90)	0.034*
Any family member with joint disease					
No	33 (57.9)	100 (87))	133 (77.3)	1	–
Yes	24 (42.1)	15 (13)	39 (22.7)	4.8(2.3, 10.3)	< 0.001*
Cigarette smoking status					
Non-smoker	22 (37.3)	63 (53.4)	85 (48)	1	–
Current smoker	26 (44.1)	45 (38.1)	71 (40.1)	1.7 (0.8, 3.3)	0.149
Ex-smoker	11 (18.6)	10 (8.5)	21 (11.9)	3.2 (1.2, 8.4)	0.022*
Physical activity					
No physical activity	36 (61)	72 (61)	108 (61)	1	–
Regular or irregular physical activity	23 (39)	46 (39)	69 (39)	1.0 (0.5, 1.9)	1.000
Educational level					
High (university or technical)/medium (high school)	29 (49.2)	88 (74.6)	117 (66.1)	1	–
Low (elementary or below)	30 (50.8)	30 (25.4)	60 (33.9)	3.0 (1.6, 5.9)	0.001*
Monthly income					
High (> US$2000)/medium (US$500–2000)	26 (45.6)	86 (76.8)	112 (66.3)	Reference	–
Low (< US$500)	31 (54.4)	26 (23.2)	57 (33.7)	3.9 (2.0–7.8)	< 0.001*
Altitude					
Mean altitude above sea level in meters	536 (SD = 57.8)	347 (SD = 38.1)			0.007*

*Statistically significant.

the presence of high knee impact repetitive movements at work was positively associated with the disease.

The final multivariable model, shown in Table 2, included the variables geographical location, BMI, type of job, family history of the disease and monthly income. Adjusting for the variables in the model, living in Bekaa was associated with the highest odds of knee OA (26.4, 95% CI: 4.3–163). Moreover, the odds for knee OA showed a significant positive trend with BMI. In particular, overweight and obese participants had

Table 2 Final multivariable logistic regression model: Lebanon, 2009

Variables	Final model Adjusted OR (95% CI)	*P*-value
Geographical location		
Beirut/Mount Lebanon	1	
Bekaa	26.4 (4.3, 163.2)	< 0.001*
North	6.5 (1.8, 24.1)	0.005*
Body mass index (BMI)		
Normal ($\leq$ 24.9 kg/m^2)	1	
Overweight (25–29.9 kg/m^2)	5.1 (1.1, 24.1)	0.039*
Obese ($\geq$ 30 kg/m^2)	8.1 (1.7, 38.2)	0.008*
Type of job		
Administrative (Office work, teaching)	1	
Manual jobs (carpenter, worker in a restaurant or in small shop)	1.6 (0.5, 5.5)	0.442
Agriculture/military	4.7 (0.9, 27.1)	0.079
Family history of the disease		
Negative	1	
Positive history of joint disease	2.73 (0.8, 9.5)	0.115
Monthly income		
High (> US$2000)/medium (US$500–2000)	1	
Low (< US$500)	1.5 (0.5, 5.0)	0.489
Goodness-of-fit	$\chi^2 = 51.4$	0.09

*Statistically significant.

significantly higher odds (5.1 and 8.1) of knee OA as compared to people with normal weight.

DISCUSSION

This study is the first step to identify risk factors for knee OA in Lebanon. It adds evidence on risks factors that are still not well established, and helps us gain understanding of the geographical disparities in its occurrence. The results are explored in relation to risk factors in depth below.

Geographical location

Participants from both the Bekaa and North governorates have higher odds of presenting with knee OA. Such geographical differences are reported in other studies, such as in the USA and China, suggesting that there might be other factors related to the disease such as local living conditions and climatic characteristics.[23,24] Interestingly, altitude above sea level (hence possibly humidity and temperature) had no role in this study when accounting for the other factors; however, further research might be warranted to reveal if part of the higher odds of the disease in North and Bekaa is due to climatic elements since these two governorates contain most of the mountainous areas in Lebanon. However, the North and Bekaa governorates were strong risk factors for knee OA despite accounting for other variables, which raises the suspicion of other factors related to these geographical disparities (as mentioned later). Even more, the attenuation of the odds of knee OA selectively for the North or Bekaa when adding type of job or family history of joint problems, respectively, highlights the potential differences in the determinants of the geographical distribution of the disease (as discussed below).

Biological/constitutional factors

The results in this study are concordant with the literature regarding the association between increased BMI and knee OA.[1,11–14] Although the increase in BMI among cases in a case-control study might be a consequence of physical inactivity due to knee OA, this was not a factor here as only incident cases were enrolled. Moreover, prospective cohort studies have shown that increased BMI antecedes knee OA, and is not due to physical inactivity secondary to the disease.[12,16] Regarding the mechanisms by which high BMI relates to knee OA, mechanical overload on the knee joint has been the classical explanation.[1] Among other systemic factors, leptin, a substance secreted by adipocites, has been identified as a determinant of degenerative intra-articular changes in knee OA.[16]

Family history of joint problems

The role of genetics in knee OA has been demonstrated in the literature, mostly for OA in the younger age groups.[17] However, in this study positive family history of joint problems was associated with the disease only at the bivariate level, losing statistical significance when place of residence was included in the final model. Since the highest rates of consanguineous marriages occur in the Bekaa governorate (one of the places associated with high odds of the disease in the final model),[29] a genetic predisposition might have an underlying role in the high occurrence of the disease. However, this variable might also indicate common living conditions shared by members of the same family. Hence, measures that are more specific should be used to identify the role

of genetic factors in the occurrence of knee OA in Lebanon.

Occupational factors

In the literature, jobs with mechanical knee overload and specific repetitive movements at work are clearly associated with knee OA.[19,30] In this study, working in military and agricultural types of jobs were significantly related to the disease only at the bivariate level, but in the presence of the North governorate in the final model, this association was not statistically significant. This could be expected since in North Lebanon, the rates of army enlistment are high as compared to other areas, and a great part of the local economy is based on agricultural practices.[31] In addition, hard working conditions and repetitive movements such as knee bending, weight-lifting and squatting are typical of military and agricultural jobs, possibly increasing the odds of knee OA among workers in such jobs.

Socioeconomic position

Although low income and educational level were not associated with knee OA in the final model, further investigation showed that this is only due to the high correlation between these variables and place of residence, in particular the North and Bekaa governorates. On the other hand, the variable monthly income lacked such correlations and was incorporated in the final model to account for its epidemiological relevance and description in the literature.[19,32,33] The dispersion of the associations when accounting for place of residence is expected, since in Lebanon, especially in underserved areas as the North and Bekaa, low income and education could be related to an increased likelihood of physically demanding jobs, inadequate nutrition and poor living conditions,[31] exposing people to musculoskeletal problems.

Behavioral factors

Smoking was not significantly related to knee OA, and this is concordant with some studies which showed no effect[32] or a negative correlation due to decreased bone density among smokers and hence less osteophyte formation in OA.[13,34] In the present study, type of leisure physical activity was not significantly associated with knee OA. This could be expected since in the literature, only the practice of sports with significant knee joint load and torsion has been related to knee OA,[21,22] and in this study, there were only few participants with such exposures.

CONCLUSIONS

After accounting for the available risk factors for knee OA in Lebanon, the OR of the North and Bekaa as compared to Beirut/Mount Lebanon remained high. This suggests that other variables might have a role in such differences, and should be explored in further studies. Some possible variables described in the literature are knee laxity, defects in knee propioception, malalignment,[1] periarticular muscle weakness,[30] and previous joint injury.[14] Other factors that could also be explored in the future are the use of oral contraceptives,[1,35] low nutritional intake of vitamins C, D and beta-carotenes,[1,36,37] high bone density,[1,14] ethnic group,[24,32,33] genetics[38] and systemic factors.[18] Moreover, we suggest exploring elements related to the social determinants of the disease, such as living conditions, local infrastructure, and access to basic health and public services. These elements tend to be underdeveloped in North and Bekaa governorates as compared to the more urbanized and modernized Beirut and Mount Lebanon,[31] and could be related to musculoskeletal overload in daily living activities. Exploring more risk factors for knee OA could increase knowledge about the occurrence of this disease and aid in planning more effective community-oriented interventions.

Strengths and limitations of the study

The study contributes to the knowledge about risk factors for knee OA in the general population rather than in specific clinical settings or in high-risk groups such as elderly women, giving valuable information about etiological factors in the community. It is also important to emphasize that the physicians clinically confirmed the outcome, and that some exposures as place of residence and BMI were not subject to recall bias because the researchers directly measured them during home visits. Moreover, the selection of incident cases allows interpreting some risk factors as obesity and overweight as most likely occurring before the onset of the outcome, and not as late consequences of musculoskeletal disability. Furthermore, since the outcome is rare, the resulting measures of association (OR) should be very similar to inherent relative risk measures, increasing their usefulness in the clinical settings and design of further larger studies.

A limitation of this study was the lack of clinical confirmation of the OA-free status of the controls, but any misclassification of a patient with early knee OA would have displaced the results toward the null. Another

limitation was the possibility of recall bias in variables such as family history of joint problems.

RECOMMENDATIONS

We recommend designing further studies, keeping in mind the ecological framework that might explain the occurrence of this disease unevenly in the Lebanese population. It seems that this type of arthritis could be a more socially determined disease than has been previously considered. Moreover, the distribution of knee OA in Lebanon might be a surrogate of important inequalities in the availability of health services and limitations in social mobility in the community.

Health authorities need to target specific occupational groups such as the military and farmers. The military training program might need a revision of the physical routines imposed on soldiers, to determine the feasibility of potential updating and changing of harmful exercises, positions, or use of physically overloading warfare equipment. Awareness programs for agricultural workers could address proper working positions and the use of alternative tools at work. Development of modern agricultural practices could decrease the physical impact of the job on farmers' health, and should be motivated (technically and economically) by government. Public health administrators should guide all these actions in order to be effective in their approach.

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