Prevalence and Risk Factors of Osteoarthritis in Madinah, Saudi Arabia, 2015 .

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ABSTRACT

Objective. According to experts of International Association on the Study of Pain, 12% of patients older than 40 years complained of pain in the joints, 50% of older people experience difficulty walking and climbing stairs, more than 15% are expressly limited mobility, and after 75 years this figure rises to 30%. The reason - is progressive degenerative lesions of joints cartilage structure or deforming osteoarthrosis (OA). Risk factors of OA can be divided into genetic (female sex, mutation of collagen II gene (COL2A1), inherited disorders of collagen II, hereditary pathology of bones and joints, ethnicity), non-genetic (age over 45, overweight, postmenopause, deficiency of vitamin D, inflammatory diseases of the joints, endocrine diseases, metabolic disorders, hypertension, hyper-uricemia, aseptic necrosis of bones, osteoporosis) and factors of environment (surgery, joint injuries, occupational stress, over-employment sports). The aim of current research was to determine the prevalence and to identify the risk factors of knee osteoarthrosis in Medina, Saudi Arabia. Methodology. The study was conducted in two stages: 1) Evaluation of the prevalence of knee OA in the King Fahd Hospital (n = 6270) – analytic retrospective study for the period July-November 2015; 2) Evaluation of clinical and anamnestic characteristics of patients with knee OA and identifying of risk factors for knee OA (the main group – with knee OA (n=220), the compare – without knee OAs (n=220)) –"case-control" study for the period July-November 2015. Socio-demographic and clinical variables was gathered by calling the patients and the filled questionnaires during the call and also by meeting the patients in the clinics. The data were entered into a unified computer database. Statistical analysis was performed using the application package IBM SPSS 20 (SPSS Inc., Chicago, USA). Results of the study showed, that the prevalence of knee OA in the King Fahd Hospital (Medina, Saudi Arabia) for the period July-November 2015 amounted to 24.88%. The study found the most important risk factors for knee OA: age more than 50 years, smoking, diabetes mellitus, trauma in past history, the number of pregnancies in anamnesis more than 10, menopause and absence of hormonal replacement therapy (HRT). Conclusions. Current research identified the main risk factors for knee OA in King Fahd Hospital in Medina, Saudi Arabia. Some of them are controllable, and some of them cannot be changed. The present study supports the need for further epidemiological and intervention studies in order to find new approaches to prevention of development and progression of knee OA.

Introduction

Involutive changes of organs and body systems, common side effects of medical treatment, the availability of competing and co morbidity - this is just a small listing of the problems faced by a doctor every day. Therefore, it is easy to imagine the importance of this issue. The problem of "aging" society necessitates the extension of active and quality of human life, which will provide the necessary social level, and lower costs for maintenance and treatment of the disabled elderly (Vyortkin A.L. et al., 2008).

According to experts of International Association on the Study of Pain, 12% of patients older than 40 years complained of pain in the joints, 50% of older people experience difficulty walking and climbing stairs, more than 15% are expressly limited mobility, and after 75 years this figure rises to 30%. The reason - is progressive degenerative lesions of joints cartilage structure or deforming osteoarthrosis (OA) (Vyortkin A.L. et al., 2008). Currently, OA is not classified as life-threatening conditions. However, chronic pain leads to reduction of life expectancy on 10-12 years on average. The duration of life of elderly patients with OA is largely dependent on intensity of pain than from the presence of concomitant life-threatening diseases (Pincus T., Sokka T., 2005). Also physical disability due to pain and limitation of functional activity of joints leads to reduced quality of life and increased risk of comorbidity and mortality (Lila A.M., 2010).

OA is a group of diseases various etiologies, with the same biological, morphological and clinical outcomes in which the articular cartilage, joint, including the subchondral bone, ligaments, capsule, synovial membrane and periarticular muscles are involved in the pathological process (Vyortkin A.L. et al., 2008). The disease occurs with equal frequency in men and women (Mozgovaya E.E., Zborovskaya E.E., 2012). OA of a knee joint is more common in women, and hip - equally often, but women have a more severe course (Prikhodko V.Y., 2011).

Knee OA or gonarthrosis, characterized by high prevalence, progressive course with early disability of the patient, as well as constant pain, essentially violating locomotor activity and contributing to development of depression, which impairs the quality of life of the patient (Svetlova M.S., 2012).

Prevalence of osteoarthrosis

Prevalence of the disease investigated in numerous epidemiological studies. OA is the most widespread form of joint disease (Vyortkin A.L. et al., 2008; Mozgovaya E.E., Zborovskaya E.E., 2012). According to for Healthcare Statistics 20% of the world population suffers from OA (Goryaev Y.A. et al., 2006).

Knee OA occurs less frequently than hand OA, more common in women, with female-to-male ratios varying between 1.5:1

and 4:1. These studies showed that severe radiographic changes affect 1% of people aged 25-34 and this figure increases in 50 times in age 75 years and more. Framingham Study found, that the prevalence of radiographic knee OA was 19.2% among participants aged over 45 years and the figure increased to 43.7% in participants of 80 years. According to the Dutch Institute for Public Health, the prevalence of knee OA in aged 55 and above was 15.6% in men and 30.5% in women. The prevalence of symptomatic knee OA is significantly lower (Bijlsma J.W.J., 2007).

Prevalence rates for knee OA, based on population studies in the US, are comparable to those in Europe (Litwic Anna et al., 2013).

In Europe there are radiographic signs of OA in most people over 65 and in 80% - over 75 years. Approximately 11% of persons older than 60 years have symptomatic OA of knee. According to a recent major studies on the epidemiology of OA in Europe (Zoetermeer Community Servey), the prevalence of knee OA by X-ray data was 14100/100 thousand in men and 22800/100 thousand in women older than 45 years (Badokin V.V., 2013).

Lawrence R.C. and colleagues (2008) showed that **US** adults age 25 and older have clinical OA of the hand, knee, or hip joint (Lawrence R.C. et al., 2008). About 19-28% of US adults age 45 or older have knee OA (Jordan J.M. et al., 2009). Among the US population older than 30 years symptomatic OA of the knee occurs in 6%, and hip joint – in 3% of population (Povoroznyuk V.V., Grigorieva N.V., 2012).

It is known that 10-17% of the population in Russia suffer from OA, a manifestation which occurs in approximately in 50 (Dosin Y.M. et al., 2011; Goryaev Y.A. et al., 2006) years of age or older, according to another authors – since 40 years (Prikhodko V.Y., 2011), and in 80 years the disease covers almost 100% of the population (Vyortkin A.L. et al., 2008).

The prevalence of knee OA in **Malaysia** is estimated at 10-20% of population (Ganasegeran K. et al., 2014), in **Spain** - 10.2% (Mas G.X., 2014).

Data on knee OA s in Asian region showed that prevalence ranged from 1.4% in urban Filipinos to 19.3% in rural communities in Iran. In India prevalence of clinically diagnosed knee OA was higher in urban (5.5%) than rural community (3.3%), but after adjusting for age and sex the prevalence was higher in rural communities (Haq S.A., 2011).

Data on the prevalence of OA, particularly of knee OA in Saudi Arabia vary widely. The study of A. Al-Arfaj and A. A. Al-Boukai (2002) found that the prevalence knee OA in Saudi Arabia is: 53.3% men and 60.9% women (Al-Arfaj A., Al-Boukai A.A., 2002). The research of Ahlberg A. and colleagues (1990) revealed that the incidence of knee and hip OA in the Primary Health Care Centre in the Eastern Province of Saudi Arabia was 3.5% (Ahlberg A. et al., 1990).

Predicted that the prevalence of OA in the population could reach 57% by 2020 (Artemenko N.A., Chvamaniya M.A., 2005).

Risk factors of osteoarthrosis
There are many factors involved in development of OA, some of them play a leading role, while others - predisposing. It should be noted that the factors associated with damage of various joints can vary significantly (Povoroznyuk V.V., Grigorieva N.V., 2012).

Risk factors can be divided into genetic, non-genetic and factors of environment (Mitrofanov V.A. et al. 2008). Genetic risk factors include female sex (Neogi T., Zhang Y., 2011; Korzh A.A. et

al., 1997), mutation of collagen II gene (COL2A1), inherited disorders of collagen II (Stickler syndrome), hereditary pathology of bones and joints (dysplasia of the femoral head, hypermobility syndrome), ethnicity (Jordan J.M. et al., 2009; Vyortkin A.L. et al., 2008; Prikhodko V.Y., 2011). Non-genetic factors include: age over 45, overweight (body mass index> 30 kg / m2) (Neogi T., Zhang Y., 2011), postmenopause, deficiency of vitamin D, inflammatory diseases of the joints (arthritis), endocrine diseases (diabetes, acromegaly et al.); metabolic disorders (gout), hypertension, hyperuricemia, aseptic necrosis of bones, osteoporosis (Vyortkin A.L. et al., 2008; Prikhodko V.Y., 2011; Kyoung Min Lee et al., 2015). Environmental factors are: surgery, joint injuries, occupational stress (for example, work of standing), over-employment sports (Mitrofanov V.A. et al. 2008).

Knee OA is caused by the interaction of multiple genetic and environmental factors. Among the many etiological factors of knee OA the greatest role play constitutional factors (age, sex, body weight, family history, reproductive characteristics) and local adverse mechanical factors (jobs, especially in everyday life, etc.) (Svetlova M.S., 2012; Nishimura A. et al., 2011).

According Dosin Y.M. and colleagues (2011), a major risk factor of primary OA - is congenital dysplasia of connective tissue in combination with overweight, leading to a mismatch between mechanical load falling on surface of articular cartilage, and its ability to resist this load (Dosin Y.M. et al., 2011).

Age. The leading risk factor for OA is the age (Blumenfeld O. et al., 2013; Vyortkin A.L. et al., 2008). Framingham Osteoarthrosis Study (2002-2005) found that in 27% of patients aged 63-70 years identified radiographic signs of OA of the knee, and the frequency increased to 44% in people over the age of 80 years. Other studies found that 80% of people older than 65 years have radiographic signs of OA (although it may be asymptomatic) (Povoroznyuk V.V., Grigorieva N.V., 2012.).

According to population studies prevalence increased 2-10 times between the ages of 30 to 65 years and continues to grow more with age (Povoroznyuk V.V., Grigorieva N.V., 2012.).

Daniel Prieto-Alhambra and colleagues (2015) showed that effect of age is the greatest for knee and hip OA in elderly Spain women (Prieto-Alhambra D. et al., 2015).

Metabolic syndrome. Obesity – is a one of major risk factor for OA of knee (Blumenfeld O. et al., 2013). Body weight increased by 3-6 times, pass through the knee joint during walking. Overloading the knee and hip joints will damage the cartilage and ligaments, as well as other support structures (Povoroznyuk V.V., Grigorieva N.V., 2012; Blidda H. et al., 2014; Widmyer Margaret R. et al., 2013).

Increased incidence of knee OA is observed at increased body weight (body mass index (BMI) greater than 25 kg/m2), and BMI greater than 27.5 kg/m2, leads to more rapid progression of knee OA (Reijman M. et al., 2006). Significant association of OA with obesity was found among women in Japan: the risk of knee OA in obesity was 2,196 times higher compared to the risk in women without obesity (Inoue R. et al., 2011). According to a meta-analysis, conducted by L. Jiang et al. (2012), increased BMI for every 5 units causes an increased risk of knee OA on 35%. Canadian scientists (2010) found that the risk of developing knee OA with BMI >30 kg / m2, 7 times higher than with BMI <25 kg / m2. In Sweden L. Lohmander et al. (2009) found that the risk of knee OA in obese patients at 8 times higher than that at normal BMI. F. Cicuttini et al. (1996) in a study of twin women of middle age found that with increasing body weight per kilogram of the risk of the disease in patients with obesity increases on 9-13%. According to a study in Norway (1991), people with a

BMI >30 kg / cm2 have the incidence of knee OA by 7.3% higher than the normal values of this parameter. In UK, D. Coggon et al. (2001) revealed that when BMI >36 kg / m2 risk of knee OA in 13.6 times higher than those with normal weight (Strebkova E.A., Alekseeva L.I., 2015). The study of Akinobu Nishimura and colleagues (2011) showed that female gender (odds ratio (OR) 2.849, 95% confidence interval (CI) 1.170-6.944) and high BMI (OR 1.243, 95% CI 1.095-1.411) were significantly associated with the frequency of knee OA in Japan population (Nishimura, Akinobu et al., 2011). A recent meta-analysis found those who were obese or overweight have a risk of incident knee OA in 2.96 times more often in comparing with those who had normal weight (95% CI 2.56–3.43). Those who had overweight but not obese had a risk of knee OA in 2.18 times more compared with normal weight people (95% CI 1.86–2.55) (Neogi T., Zhang Y., 2011).

Hilde Apold and colleagues (2014) showed that there are relationships between BMI and heavy labour, and knee OA. In the highest versus of BMI relative risk was 6.2 (95% CI: 4.2-9.0) in men and 11.1 (95% CI: 7.8-15.6) in women. Men with heavy labour at work had a relative risk of OA - 2.4 (95% CI: 1.8-3.2), corresponding figure in women was 2.3 (95% CI: 1.7-3.2). The effect of BMI and physical activity at work was additive in men and women (Apold H., 2014).

Asfandiyarova N.S. and colleagues (2013) found that OA in patients with diabetes type 2 develops earlier than in general population, but after 60 years, the difference disappears (Asfandiyarova N.S. et al., 2013).

Chang Dong Han and colleagues (2013) found that high waist circumference was associated with knee OA in Korean female (Han, Chang Dong et al., 2013).

Sartori-Cintra A.R. et al. (2014) concluded that obesity is a risk factor for OA, but physical activity and diet can reduce the progress or prevent the disease (Sartori-Cintra A.R. et al., 2014).

Stella G. Muthuri and colleagues (2011) conducted a meta-analysis of studies on obesity as risk factors for knee OA, as well as assessed the potential reduction of the risk by controlling this risk factor. Meta-analysis showed that the total combined OR for overweight and obese individuals were 2.02 (95% CI = 1.84-2.22) and 3.91 (95% CI = 3.32-4.56), respectively. Reducing of risk for knee OA ranged from 8% in China to 50% the United States, depending on the prevalence of overweight and obesity. Thus, the authors concluded that obesity is a risk factor for knee OA. But its advantage is that it is controllable, and that weight loss can lead to a significant reduction of knee OA risk in general population, especially in Western countries, where obesity is common (Muthuri S.G. et al., 2011).

Yoshimura N. and colleagues (2012) showed association between the occurrence knee OA and components of metabolic syndrome, including overweight, hypertension, dyslipidaemia, and impaired glucose tolerance, in a general population. The study revealed that the OR for occurrence of knee OA significantly increased according to number of metabolic syndrome components (for one component OR=2.33; two components - 2.82; three components - 9.83) (Yoshimura N. et al., 2012).

Status of endocrine system. Currently, it is proved that hormones are important regulators of growth and development of cartilage tissue and chondrocytes have specific receptors for thyroxin, insulin, glucocorticoids, somatotropin, estradiol, and testosterone. Experimental studies have established that hormone imbalance in the body leads to a change in metabolism of cartilage, and therefore disturbances in endocrine system can be regarded as a risk factor of OA (Povoroznyuk V.V., Grigorieva N.V., 2012).

Mariely Nieves-Plaza and colleagues (2013) showed, that patients with diabetes mellitus had 2.18 the odds of OA in comparing to non diabetic patients (95% CI: 1.12–4.24), sub-analysis among diabetes mellitus patients showed, that female patients were more likely to have hand or knee OA (OR=5.06, 95% CI=1.66-15.66) (Nieves-Plaza M. et al., 2013).

To date in the world literature there is a discussion about the role of sex hormones deficiency and menopause in development of OA. A meta-analysis of Nevitt M.C. and Felson DT (1996) of four researches concerning risk of knee and hip OA in women taking hormone replacement therapy showed that the relative risk (RR) of OA lower and amounts 0.76; 95% confidence interval (CI): 0,63-0,91 (Povoroznyuk V.V., Grigorieva N.V., 2012).

Excessive stress on joints. The character of work and sports also effect specificity of manifestations of OA in different joints (Korzh A.A. et al., 1997). Important risk factor of OA is excessive load on the joint (Ezzat Allison M. et al., 2013). Professional load associated with knee flexion, squatting and stair climbing are associated with a higher risk of developing OA of the knee, while lifting weights, heavy physical work associated with the risk of coxarthrosis (Palmer Keith T., 2012). Professional athletes participating in competitions in contact sports, have an increased risk of OA of the knee due to the primary weakness of the quadriceps - a risk factor for development of OA a result of lower joint stability and reducing absorption properties of muscles at loadings. The risk of OA is increased in those who participate in certain sports, including wrestling, boxing, pitching in baseball, cycling, parachuting, cricket, gymnastics, ballet dancing, soccer, and football; by contrast, running does not appear to increase the risk of OA. Thus, it found that OA is more common in persons engaged in heavy physical labor, and with the experience of more than 5 years (Povoroznyuk V.V., Grigorieva N.V., 2012).

McWilliams D.F. and colleagues (2011) made a systematic review of observational studies of knee OA and occupation (job, sport, heavy work, kneeling, and other activities). Study designs showed a positive association between knee OA and occupational activities: cohort (OR 1.38, 95% CI 1.10-1.74), cross-sectional (OR 1.57, 95% CI 1.37-1.81) and case control (OR 1.80, 95% CI 1.48-2.19). The authors concluded that some occupational activities increase the risk of knee OA; however the influences of publication bias and heterogeneity can limit this study (McWilliams D.F. et al., 2011).

Genetic factors. Genetic factors play an important role in the high prevalence of gonarthrosis, which is confirmed by a high index of inheritance of the disease (0,39-0,65 among twins), regardless of predisposing environmental factors or demographic characteristics (Jordan K.M. et al., 2003).

Meta-analysis of Suotang Kou and Yaochi Wu (2014) suggested that AA and GA genotypes of TNF- -308 increase risk of knee OA in comparing with GG genotype, which may be explained by higher expression of TNF- , which induces osteoclastic bone resorption and destruction of cartilages, in the -308A allele carriers than in the -308G carriers (Kou S., Wu Y., 2014).

Meta-analysis of Jin-Ming Shen and colleagues (2014) suggested that mtDNA haplogroup J and cluster TJ correlate with risk of OA in Spanish population (Shen Jin-Ming et al., 2014).

Suliang Lou and colleagues (2014) demonstrated that presence of ADAM12 rs1871054 variant significantly associated with increasing of OA susceptibility in Chinese Han population (Lou S. et al., 2014). Poonpet T. and colleagues (2013) showed that the nsSNP rs4747096 polymorphism of ADAMTS14 gene was associated with knee OA in female Thai patients (Poonpet T. et al., 2013).

The study of Hsin-Yi Yang and colleagues (2014) suggested that the FN-1 rs940739A/T polymorphism may be an important risk factor of genetic susceptibility to knee OA in the Han Chinese population (Yang Hsin-Yi et al., 2014).

Lifestyle (education, smoking, diet, physical activity, parity). Kyoung Min Lee and colleagues (2015) found high level of education as a protective factor of OA among South Korean older adults (Kyoung Min Lee et al., 2015).

There are conflicting data about effect of smoking on OA. There are studies identified a low risk of OA associated with smoking (Mnatzaganian G. et al., 2013), and a study found an inverse relationship between the duration of smoking and knee OA (Mnatzaganian G. et al., 2011). Other studies have found no association (Wilder F.V. et al., 2011; Hui, M. et al., 2011).

Published data about relationship between physical activity and knee OA are contradictory (Felson David T. et al., 2013). Some studies suggest that high physical activity increases the risk of knee OA (Wang Y. et al., 2011), while others show the opposite effect (Rogers L.Q. et al., 2002), and others - that have no effect (Felson, D.T.). The author suggests that the risk of OA depends on the type and position of physical activity (Felson David T. et al., 2013).

Dorothy D. Dunlop and colleagues (2014) conducted a multi-center study, which showed that the constant daily light physical activity reduces risk of disability in patients with OA (Dunlop D.D. et al., 2014). Kathryn R. Martin and colleagues' (2013) study found that more active individuals (both at work and in their spare time) have a lower risk of knee OA than those who are less active (Martin Kathryn R. et al., 2013). On the other hand Edwards M.H. et al. (2014) showed that clinical knee OA, hip OA, or both were associated with poor physical performance - OR (95%CI) 2.93(2.36;3.64), 3.79(2.49;5.76), and 7.22(3.63;14.38) respectively (Edwards M.H. et al., 2014).

Low temperature environmental factor has an adverse effect on the human body, including the joints. The lower limbs and especially the knee joints are most prone to hypothermia. The reasons for this are both features of labor outdoors, and local circulation of the joint tissues, as well as the nuances of the current work clothes. According to a study of Malchevskiy V.A. and Petrov S.A. the impact of low-temperature factor on men working in the Far North leads to a sharp increase of the incidence of knee OA (Malchevskiy V.A., Petrov S.A., 2013).

Jørgensen K.T. and colleagues (2011) showed that the risk of knee OA in Danmark was highest among married persons and persons with low education or low income, also in women with pregnancy and delivery in past history (Jørgensen K.T. et al., 2011). Wise Barton L. and colleagues (2013) showed that women with parity more than 4 have risk for knee OA (OR 2.6, 95% CI: 1.2; 5.3) (Wise Barton L. et al., 2013).

The role of vitamin D deficiency in the pathogenesis of OA remains controversial. Two epidemiologic studies found that low levels of vitamin D in serum have been associated with increased risk of hip and knee OA, but there is no conclusive evidence that vitamin D deficiency is a risk factor for knee OA (Sanghi Divya et al., 2013).

Joint injuries. Post-traumatic OA occurs following traumatic joint damage, when the articular surface is disrupted, resulting in instability of the joint. Risk OA after joint trauma reaches 75%, and intraarticular fractures may increase the risk more than 20 times (Schenker Mara L. et al., 2014). According to Blagojevic M. and colleagues (2010) knee injury confers a 4-fold increased risk of knee OA (Blagojevic M. et al., 2010). Muthuri S.G. and colleagues (2011) consider that knee injury in the past history is a major risk factor for development of knee OA (Muthuri S.G. et al., 2011).

Ethnicity. In a number of few studies was found that OA more common in women black race than in European race women (Svetlova M.S., 2012).

Jordan J.M. and colleagues (2009) showed that African Americans overall as well as African American men had higher prevalence of radiographic hip OA than Caucasians (32.1% vs. 26.6%, and 32.2% vs. 23.8%, respectively), while there was no difference between African American and Caucasian women (40.3% vs. 39.4%) (Jordan J.M. et al., 2009).

Context of the problem
Osteoarthrosis is the most common rheumatic disease, which leads to disruption of the functional capacity of the musculoskeletal system, disability, and represents a great medical and social problem. Today there are a huge number of diverse studies related to OA. However, there are not enough researches about prevalence, structure, and risk factors in Arab world, or there is outdated information.

Purpose of the Study
The aim of the study was to determine the prevalence and to identify the risk factors of knee osteoarthrosis in Medina, Saudi Arabia.

Research Questions
1. What is the prevalence of knee osteoarthrosis in King Fahd Hospital in Medina, Saudi Arabia?
1. What are the risk factors of knee osteoarthrosis King Fahd Hospital in Medina, Saudi Arabia?

Significance of the Study
Definition of prevalence and identification of risk factors for knee osteoarthrosis in Saudi Arabia is necessary for activities to prevent disease, reduce the rate of progression, and the frequency of disability.

Research hypothesis
- The prevalence of knee osteoarthrosis in the King Fahd Hospital (Medina, Saudi Arabia) for the period July-November 2015 amounts to 25%
- he main risk factors of knee osteoarthrosis are age, body weight, somatic diseases such as diabetes mellitus, heavy stress on joins, traumas in past history, menopause and parity in women

Definition of Terms
Osteoarthrosis – is a group of overlapping various diseases of different etiology that have the same biological morphological and clinical outcome, in which pathological process involves not only the articular cartilage, but the entire joint, including the subchondral bone, ligament, capsule, synovial membrane and periartikular muscles (Nasonova V.A. et al., 2011)

Risk factor – age, body weight, somatic diseases such as diabetes mellitus, heavy stress on joins, traumas in past history, menopause and parity in women.

Prevalence of disease – is the percentage of population, which were the cases of disease for a certain period of time (Coggon D. et al., 1997).

Methodology
Design of the study
All study activities was approved by the Ethics committee for Ethical review and conducted on the basis of the King Fahd Hos-

pital from July to November 2015. The study was conducted in two stages; they are shown in Figure 1.
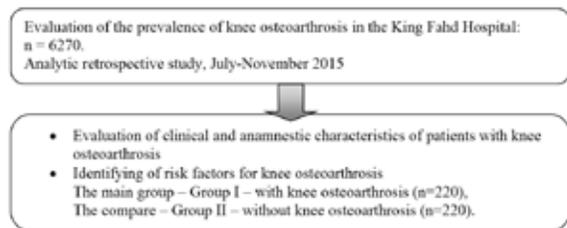

Figure 1 - The main stages of the study

To determine the prevalence and structure of knee OA in the King Fahd Hospital for the period July-November 2015, a retrospective analytical study was conducted on the **first stage**. The total number of analyzed patients' histories of current study was 6270.

Clinical and anamnestic features of patients with knee OA and risk factors were identified in a "case-control" study on the **second stage**. There were two groups of patients, accepted by the King Fahd Hospital (patients with knee OA – the main group, and without knee OA – the compare group), each group consisted of 220 people.

Settings of the study

Socio-demographic and clinical variables was gathered by calling the patients and the filled questionnaires during the call and also by meeting the patients in the clinics . After that, they were invited to voluntary informed consent, which explains the essence and the methodology of the study. Then, with the consent of patients to participate in the study, they were divided into two groups (Group I or Group II), according to criteria of including and excluding. In case of refusal of the patient to participate in research at any stage, the patient was excluded from the research.

All patients, included in the study, were interviewed according to the questionnaire which we developed. The questionnaire included 40 questions, covering 73 possible risk factors for knee OA, and providing information about demographic data (1-3 questions), clinical characteristics (4-5 questions), physical activity (6-8 questions), occupation (9-16 questions), anamnesis of the patient and treatment (17-18, 21-32, 34 questions), bad habits (19-20 questions), heredity (33), and questions for women (35-40 questions).

Sample of the study

440 patients, accepted by the King Fahd Hospital (Medina, Saudi Arabia) for the period July-November 2015, were enrolled in the study.

$$n = \frac{(z_{\alpha/2})^2 p(1-p)}{\Delta^2}$$ w was used to calculate the sample size:

At a confidence level of 95% and confidence interval 5% the minimum sample size was calculated as 362.

Criteria of including and excluding showed in the table 1.

Table 1 – Criteria of including and excluding

Criteria of including	
The main group (Group I) – with knee OA	The compare group (Group II) – without knee OA
Age more than 18 years Knee osteoarthrosis Absence of other types of osteoarthrosis Absence of disease in decompensation or noncontroled disease Agreement to participate in research	Age more than 18 years Absence of knee osteoarthrosis Absence of other types of osteoarthrosis Absence of disease in decompensation or noncontroled disease Agreement to participate in research
Criteria of excluding	
Age less than 18 years Absence knee osteoarthrosis Other types of osteoarthrosis Heavy disease of organs and systems Lack of consent to participate in research	Age less than 18 years Knee osteoarthrosis Other types of osteoarthrosis Heavy disease of organs and systems Lack of consent to participate in research

Method of data collection

The data in this study was gathered by calling the patients and the filled questionnaires during the call and also by meeting the patients in the clinics . 440 questionnaires, characterizing socio-economical, somatic, obstetrical and gynecological (for women) features, as well as lifestyle characteristics of object of the study, were analyzed. The data were entered into a unified computer database.

Statistical Analysis

Statistical analysis was performed using the application package IBM SPSS 20 (SPSS Inc., Chicago, USA). The character of data distribution was evaluated with W-criterion of Shapiro-Wilk. Various algorithms of statistical analysis were used depending on the type of distribution of feature. Absolute and relative indicators (%) were used to represent the qualitative characteristics. A comparison of two independent groups on one or several signs, having at least one of the groups of distribution different from the normal, or if the type of distribution was not analyzed, was carried out by checking the statistical hypotheses about the equality of middle rank using the Mann-Whitney U-test. Comparison of 3 independent samples was performed using Kruskal-Wallis criterion. Analysis of contingency tables (2) was used to assess the differences of relative values. Fisher exact p was applied at frequencies less than 5 (Minko A.A., 2004). Comparison of the relative frequencies in two groups was carried out by comparing the 95% confidence interval (CI) relative frequencies. If the CI did not overlap, then frequencies were significantly different (with significance level 0.05). If the intervals overlapped, the differences were not statistically significant. Checking of the null statistical hypothesis about the equality of relative frequencies in two groups also was performed (Shmoilova R.A et al., 2011).

The formula below was used to assess the impact of each factor on the risk of knee OA:

OR = AD / BC ,

where A - the number of individuals from the group of patients with knee OA who have studied traits; C - the number of individuals from the group of patients with knee OA, not having studied traits; B - the number of persons from the group of patients without knee OA who have studied traits; D - the number of persons from the group of patients without knee OA, not having studied traits.

Chi-square ($\chi 2$) was used to test the hypothesis of no difference. 95% CI for the odds ratio (OR) was calculated by Woolf method to demonstrate the strength of correlation. The formula below was used for it:

ln (OR) ± t× ,

where ln (OR) – the value of the natural logarithm of odds ratio;

t – the value of the t-test for independent samples.

CI was obtained after conversion of the lower and the upper limit by raising of the number e to a power of the values of limit. If the CI for the OR included 1.0, then the differences between groups in studied traits were not statistically significant. If all values of CI were more than 1.0, then the studied traits were risk factors. In case CI less than 1.0 - the trait was a factor of stability, and if OR=1.0, then a trait did not has risk significance (Rebrova O.Yu., 2002).

Limitations of the study
A study was conducted on basis of one hospital and cannot characterize the population of Saudi Arabia in general.

Results of the study
Evaluation of clinical and anamnestic characteristics of patients with knee osteoarthrosis
To evaluate the clinical and anamnestic features of patients with knee OA case-control study was conducted. Brief characteristics of the patients Group I and Group II are presented in Tables 2 and 3.

Both groups were represented by women more than in 80% of cases, but statistical significantly difference in gender structures between two groups was not found (95%CI [74.71-85.29] and [82.34-91.28], x^2=3.136, p=0.077).

Age structure of studied groups showed on figure 2. The main group was represented by patients aged more than 30 years in 85% of cases that makes it different from the control group, where the similar figure did not exceed 35% (x^2=145.564, p<0.0001).

Group I - with knee OA

■ less than 30 ■ 30-50 □ more than 50

\s

Group II - without OA
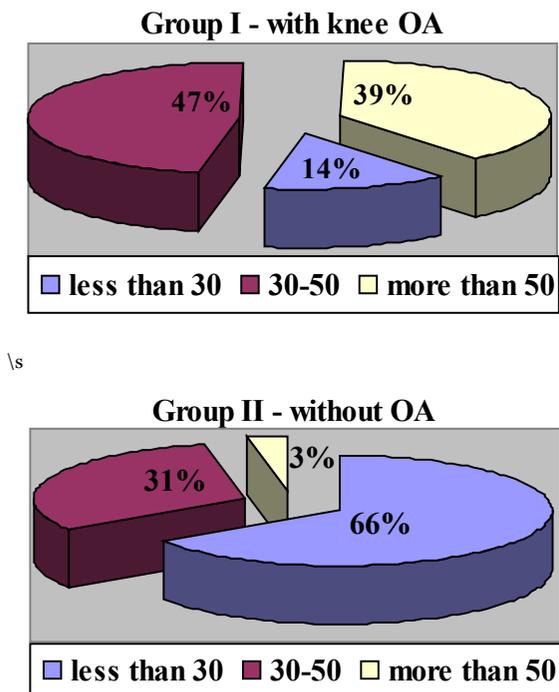

■ less than 30 ■ 30-50 □ more than 50

\s

Figure 2 – Age structure of studied groups

More than 60% of patients with knee OA had weight over 71 kg, while 75% of patients had height less than 165 cm. These figures were significantly different from the respective figures of the

comparison group (x^2=29.720, p<0.0001 and x^2=11.457, p=0.009, respectively).

Among patients with knee OA 13% were smokers, the same figure in the Group II was less by 3 times (95%CI [8.71-17.65] and [1.80-7.30], x^2=12.608, p<0.0001).

Table 2 – Brief characteristics of the patients both groups

Variable	Group I with knee OA, n=220		Group II without knee OA, n=220		x^2	p
	%	95%CI	%	95%CI		
Gender female male	80.00 20.00	74.71-85.29 14.71-25.29	86.81 13.19	82.34-91.28 8.72-17.66	3.136	0.077
Age (years) less than 30 30-50 more than 50	14.09 47.28 38.63	**9.49-18.69** **40.68-53.88** **32.20-45.06**	65.45 31.36 3.18	**59.17-71.73** 25.23-37.49 0.86-5.50	145.564	0.000
Weight (kg) less than 50 50-70 71-90 more than 90	8.4 30.91 42.27 18.18	**4.93-12.35** 24.8-37.02 **35.74-48.8** 13.08-23.28	22.73 38.18 28.18 10.91	**17.19-28.27** 31.76-44.60 **22.24-34.12** 6.19-14.19	29.720	0.000
Height (cm) less than 150 150-165 166-175 more than 175	23.66 52.75 19.02 4.57	**18.03-29.27** **46.15-59.35** 13.83-24.21 1.81-7.33	13.18 69.10 10.91 6.81	**8.71-17.65** **62.99-75.21** 6.79-15.03 3.48-10.14	**11.457**	**0.009**
Smokers	13.18	8.71-17.65	4.55	1.80-7.30	12.608	0.000
Somatic diseases	40.91	34.41-47.41	24.09	18.44-29.74	13.808	0.000
Diabetes mellitus	19.55	14.31-24.79	8.18	4.56-11.80	10.864	0.001
Trauma in past history (car accidents, falling from high place, direct trauma to joint etc.)	24.09	18.44-29.74	0.45	0-1.33	58.825	0.000
Family history of osteoarthrosis	42.27	35.74-48.80	39.09	32.64-45.54	0.417	0.518

Among participants of the Group I 40% had somatic diseases that was 1.5 times more than in the Group II (95%CI [34.41-47.41] and [18.44-29.74], x^2=13.808, p<0.0001).

About 25% of patients with OA reported about severe injuries in their past history, the same figure in patients without OA was less than 1% (95%CI [18.44-29.74] and [0-1.33], x^2=58.825, p<0.0001).

Brief characteristics of women in Group I and Group II are presented in Table 3.

About 90% of women in the main group were married and had pregnancy in anamnesis, while these figures in compare group was about 50% (x^2=54.922, p<0.0001 and x^2=59.237, p<0.0001, respectively).

One third of women from the Group I had menopause that was 6 times more than in the Group II (95%CI [26.43-40.63] and [1.93-8.65], 2=29.760, p<0.0001). However, about 4% of women of the Group I received hormone replacement therapy, whereas this indicator in the comparison group was 17% (95%CI [1.13-7.11] and [11.41-22.71], 2=5.196, p=0.023).

Table 3 – Brief characteristics of women in both groups

Variable	Group I with knee OA, n=170		Group II without knee OA, n=170		2	p
	%	95%CI	%	95%CI		
Married	88.24	83.40-93.08	50.00	42.48-57.52	54.922	0.000
Pregnancy in past history	86.47	81.33-91.61	46.47	38.97-53.97	59.237	0.000
Menopause	33.53	26.43-40.63	5.29	1.93-8.65	29.760	0.000
Hormonal replacement therapy	4.12	1.13-7.11	17.06	11.41-22.71	5.196	0.023

Thus, most of patients with knee OA were older than 30 years. They are more often were obese, had medical comorbidity and trauma history. The vast majority of women in the main group was married and had a history of pregnancies. The number of women in menopause was higher than in comparison group. However, the percentage of patients receiving hormone replacement therapy in comparison group was significantly higher.

Evaluation of the prevalence of knee osteoarthrosis in the King Fahd Hospital, Saudi Arabia
To evaluate the prevalence of knee OA in the King Fahd Hospital analytic retrospective study was conducted. Current study included analysis of 6270 medical histories of patients who sought for medical care to the King Fahd Hospital (Medina, Saudi Arabia) during the period July-November, 2015.

The average number of patients with knee OA accounted 14.67 ± 6.35 per day. **Thus**, the prevalence of knee OA in the King Fahd Hospital (Medina, Saudi Arabia) for the period July-November 2015 amounted to 24.88%. These figures are slightly higher than the data Framingham Study, conducted in 2007, which showed, that the prevalence of knee OA was 19.2% among participants aged over 45 years. However, according to a study of Artemenko N.A. and Chvamaniya M.A. (2005), the prevalence of knee OA tends to increase and is projected in 2020 will be 57%. On the other hand the findings differ from similar studies conducted Ahlberg A. and colleagues (1990) and Al-Arfaj A. and Al-Boukai A.A. (2002) in Saudi Arabia, where the rate of knee OA was 3.5% and 60%, respectively. This may be due to sample size and to the size of area covered by studies.

Identification of risk factors for knee osteoarthrosis in the King Fahd Hospital (Medina, Saudi Arabia)
To determine risk factors for knee OA a "case-control" study was carried out, it included 440 patients (the main group - 220 patients with knee OA, the comparison group - 220 patients without OA). The total number of studied factors was 73. Risk factors for knee OA reported in Table 4.

It is known than age – is a one of the main risk factors for OA (Blumenfeld O. et al., 2013). The study showed than age more than 30 years increases the risk of knee OA about 2 times, however age more than 50 years raises it 19 times (OR=19.16, 95%CI[4.52-22.85]). These data are similar to literature data (Povoroznyuk V.V., Grigorieva N.V., 2012; Prieto-Alhambra D. et al., 2015), which reported that the risk of OA is directly proportional to the patient's age.

According to meta-analysis, conducted by Neogi T. and

Zhang Y. (2011), those, who were overweight, had a risk of knee OA 3 times more. Current research confirmed these data and revealed that weight more than 70 kg is a risk factor and increases the chance to have knee OA in more than 2 times (OR=2.38, 95%CI[1.62-3.49]).

Active smoking causes a reduction of bone mineral density, which in turn contributes to OA. Furthermore it is known that bone tissue containing estrogen receptors, is highly sensitive to estrogens. Estrogens inhibit bone resorption, while the ingredients of tobacco smoke is not only reinforce it, but also inhibit bone formation. Calcitonin resistance and impaired vitamin D metabolism occurs Along with estrogen deficiency and also reduces of bone mineral density. Some of the chemical elements which are a part of tobacco smoke are the calcium antagonists and may join with it in a competitive relationship (Dyubkova T.P., 2008). However, despite the fact that literature data regarding the effect of smoking on the incidence of OA rather inconsistent (Mnatzaganian G. et al., 2011, 2013; Wilder F.V. et al., 2011; Hui, M. et al., 2011), our study showed that the risk of knee OA among smokers is 3 times higher (OR=3.19, 95%CI[1.51-6.72]).

The presence of somatic diseases as diabetes mellitus increases the chance of knee OA 2.7 times (OR=2.73, 95%CI [1.52-4.90]). These data are consistent with data obtained Mariely Nieves-Plaza and coll. (2013) that diabetes mellitus increases the risk of knee OA more than 2 times. However, if to consider the impact of health status on the risk of knee OA, we can say, and this is confirmed by our study that the strongest risk factor is a history of injuries (OR=69.50, 95%CI[9.51-507.75]). And this confirmed by literature data (Blagojevic M. et al., 2010; Muthuri S.G. et al., 2011). So according to Schenker Mara L. and coll. (2014) the risk of OA after trauma reaches 75% and raises 20 times after intraarticular fractures (Schenker Mara L. et al., 2014).

No doubt that character of work and lifestyle influence on the occurrence of some diseases. A huge amount of researches about the relationship of labour, participation in physical training, and other kinds of activities and OA were carried out, but published data about it are contradictory (Felson David T. et al., 2013). Some authors conclude that high physical activity contributes to manifestation of OA (Wang Y. et al., 2011), other studies suggest the opposite (Rogers LQ et al., 2002), and the third - about the lack of any correlation (Felson David T. et al., 2013). However, most authors conclude that the risk of OA depends on the type and position of physical activity (Felson David T. et al., 2013). Thus, according to Palmer Keith T. (2012) and Povoroznyuk V.V. and Grigorieva N.V. (2012) professional load associated with knee flexion, squatting, stair climbing, lifting weights, heavy physical work is associated with a higher risk of developing OA of knee. On the other hand Dorothy D. Dunlop and coll. (2014) and Kathryn R. Martin and coll. (2013) found that light daily physical activity and running reduce the risk of OA and the risk of disability in with OA. And Edwards M.H. and coll. (2014) showed that poor physical performance increases the risk of knee OA 3 times. Current study showed that sport walking, running and weight lifting increase the risk of knee OA 1.8 time (OR=1.78, 95%CI[1.21-2.62]), but squatting, climbing stairs, kneeling, and work, associated with heavy lifting (over 10 kg), were not a risk factors (OR=1.10, 95%CI[0.72-1.67]; OR=0.80, 95%CI[0.55-1.17]; OR=0.93, 95%CI[0.55-1.58], and OR=1.54, 95%CI[0.97-2.43], respectively) . At the same time, long-term being in sitting position and the lack of daily activity increases the chance of knee OA 1.8 and 2 times respectively (OR=1.77, 95%CI[1.17-2.69] and OR=2.18, 95%CI[1.18-4.04]). On the other hand, daily light exercise and walking more than 2 km are the factors of stability (OR=0.46, 95%CI [0.25-0.85] and OR=0.45, 95%CI [0.27-0.76], respectively).

Table 4 – Risk factors for knee osteoarthrosis

№	Risk factor	The frequency of risk factor		OR	95% CI	p
		Group I knee OA n=220	Group II without OA n=220			
1	Female sex	176	191	0.60	0.36-1.01	0.0560
2	Male sex	44	29	1.65	0.99-2.75	0.0560
3	Age less than 30 years	31	144	0.09	0.05-0.14	<0.0001
4	30-50 years	104	69	1.96	1.33-2.89	0.0007
5	more than 50 years	85	7	19.16	4.52-22.85	<0.0001
6	Weight less than 50 kg	19	50	0.32	0.18-0.56	0.0001
7	more than 50 kg	201	170	3.11	1.77-5.48	0.0001
8	50-70 kg	68	84	0.72	0.49-1.07	0.1090
9	more than 70 kg	133	86	2.38	1.62-3.49	<0.0001
10	71-90	93	62	1.87	1.25-2.78	0.0021
11	more than 90 kg	40	24	1.81	1.05- 3.13	0.0321
12	Height less than 150 cm	52	29	2.04	1.24-3.36	0.0052
13	more than 150 cm	168	191	0.49	0.30-0.81	0.0052
14	150-165 cm	116	152	0.50	0.34-0.74	0.0005
15	less than 165 cm	168	181	0.70	0.44-1.11	0.1270
16	166-175 cm	42	24	1.93	1.12-3.31	0.0175
17	more than 175 cm	10	15	0.65	0.29-1.48	0.3063
18	Smoking	29	10	3.19	1.51-6.72	0.0023
19	Daily physical exercises	17	34	0.46	0.25-0.85	0.0129
20	absence of it	203	186	2.18	1.18-4.04	0.0129
21	Sport walking, running or weightlifting	101	71	1.78	1.21-2.62	0.0035
22	Seating position for more than 2 hours a day	168	142	1.77	1.17-2.69	0.0069
23	Standing position for more than 2 hours a day	145	134	1.24	0.84-1.83	0.2766
24	Squatting position for more than 1 hour a day	62	58	1.10	0.72-1.67	0.6686
25	Kneeling position for more than 1 hour a day	33	31	0.93	0.55-1.58	0.7869
26	Walking more than 2 km daily	25	49	0.45	0.27-0.76	0.0026
27	Climbing up more than 30 steps a day	96	108	0.80	0.55-1.17	0.2515
28	Lifting weights over 10 kg a working day	56	40	1.54	0.97-2.43	0.0658
29	Somatic diseases	90	53	2.18	1.45-3.29	0.0002
30	Vitamin D Deficiency	92	83	1.19	0.81-1.74	0.3808
31	Diabetes mellitus	43	18	2.73	1.52-4.90	0.0008
32	Trauma in past history (car accidents, direct trauma to joint etc.)	53	1	69.50	9.51-507.75	<0.0001
33	Bone deformations	13	5	2.7	0.95-7.71	0.0634
34	Muscles weakness	71	40	2.14	1.37-3.34	0.0008
35	Any types of disability	9	3	3.09	0.82-11.55	0.0944
36	Family history of OA	93	86	1.14	0.78-1.67	0.4970

According to the study women do not have a higher risk of knee OA (OR=0.60, 95%CI [0.36-1.01]). But assessment of some states demonstrated that women have additional risk factors for knee OA. Risk factors for knee OA among women reported in Table 5.

Marital status and parity, as it turned, can also influence the development of OA. The study found that married women have a higher risk of knee OA (OR=7.5, 95%CI [4.30-13.07]). In addition the presence of more than 5 pregnancies in anamnesis increased the risk 6.5 times (OR=6.51, 95%CI [3.66-11.57]) and the presence of more than 10 pregnancies – more than 12 times (OR=12.84, 95%CI [1.65-99.86]). These data are consistent with the literature data, since the study of Jørgensen K.T. and coll. (2011) showed that the risk of knee OA was highest among married persons, also in women with pregnancies and deliveries in past history. And Barton L. and coll. (2013) revealed that women with parity more than 4 have 2.6 times more chances for knee OA.

Table 5 – Risk factor of knee OA among women

№	Risk factor	The frequency of risk factor		OR	95% CI	p
		Group I knee OA n=170	Group II without OA n=170			
1	Married	150	85	7.50	4.30-13.07	<0.0001
2	Pregnancy in anamnesis	147	79	7.36	4.32-12.54	<0.0001
3	less than 5	61	60	1.03	0.66-1.60	0.91
4	5-10	74	18	6.51	3.66-11.57	<0.0001
5	more than 10	12	1	12.84	1.65-99.86	0.0148
6	Menopause	57	9	9.02	4.29-18.97	<0.0001
7	since less than 30 years	2	0	0.48	0.05-5.16	0.5463
8	since 30-40 years	11	1	1.91	0.22-16.93	0.5598
9	since 40-50 years	16	4	0.48	0.12-2.05	0.3272
10	since more than 50 years	28	4	1.21	0.29-4.96	0.7943
11	Hormonal replacement therapy	7	29	0.21	0.09-0.49	0.0003
12	absence of it	163	141	4.79	2.04-11.27	0.0003
13	High heels	60	90	0.48	0.31-0.75	0.0011

It is proved that hormones play a great role in development of several diseases, including OA. Studies showed that hormone disorders in menopausal women increase the risk of OA, whereas hormonal replacement therapy (HRT) helps to reduce it (Nevitt M.C., Felson D.T., 1996; Povoroznyuk V.V., Grigorieva N.V., 2012). Current study showed that menopause increased the risk of knee OA 9 times (OR=9.02, 95%CI [4.29-18.97]), but the age of it had no effect on raising the risk (95%CI included 1). At the same time HRT was a protective factor (OR=0.21, 95%CI [0.09-0.49]), and absence of it increased the chance of developing of knee OA more than 4 times (OR=4.79, 95%CI [2.04-11.27]).

Interesting results were obtained with respect to wearing high heels. The study found that wearing high heels reduced the risk of knee OA (OR=0.48, 95%CI [0.31-0.75]). Perhaps this is the equivalent of a light physical activity and strengthens the muscles, whereas its weakness leads to increasing the risk of knee OA more than 2 times (OR=2.14, 95%CI [1.37-3.34]).

Thus, the study found the most important risk factors for knee OA, and they are shown in Table 6.

Table 6 – The main risk factors of knee OA

Risk factor	OR
Age more than 50 years	19.16
Weight more than 70 kg	2.38
Smoking	3.19
Diabetes mellitus	2.73
Trauma in past history	69.50
The number of pregnancies in anamnesis 5-10	6.51
The number of pregnancies in anamnesis more than 10	12.84
Menopause	9.02
Absence of HRT	4.79

Conclusions and recommendations

The strategic objectives of the management of patients with OA are slowing the progression of the disease, prevention of deformities and disability, pain relief, suppression of inflammation, reducing the risk of relapse and destruction of the joints, and improvement of life quality. But the most important is timely detection of OA risk factors and preventive measures in high-risk group. The relevance of enhancing effectiveness of prevention and treatment of OA is associated with the fact that the population of developed countries is getting old and, consequently, the number of people suffering from OA, increases (Mitrofanov V.A. et al. 2008).

Despite the enormous amount of research, our knowledge about risk factors of OA is not sufficient. Methodological difficulties hinder an understanding of etiology of the disease, especially in progression of OA. Therefore, prevention of OA remains difficult (Jordan J.M. et al., 2011).

The research evaluated that the prevalence of knee OA in King Fahd Hospital in Medina (Saudi Arabia) for the period July-November 2015 was to 24.88%. Current research identified the main risk factors for knee OA in in King Fahd Hospital in Medina, Saudi Arabia. Some of them are controllable, such as body weight, bad habits (smoking) and the number of pregnancies and labors, and some of them cannot be changed, such as age,

concomitant diseases and injuries, and menopause in women. However, along with the identified risk factors the protective factors were distinguished: daily light physical activity, taking HRT, and wearing high heels for women.

Into account the identified risk factors to prevent OA can be recommended: avoid stress on joints (lifting and carrying heavy loads, and traumas), avoid long sitting in a fixed pose, diet (low fat, but enough whole grains, fruits and vegetables which contain vitamins, minerals and cellular tissue, eating small meals 5-6 times a day), active lifestyle (daily walking on flat terrain at a moderate pace for 30-60 minutes, regular health improving gymnastics, swimming), the fight against smoking, and taking HRT for women according to indications.

The present study supports the need for further epidemiological and intervention studies in order to find new approaches to prevention of development and progression of knee OA.

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