

**USE OF TRADITIONAL AND COMPLEMENTARY
MEDICINE AND ITS ASSOCIATED FACTORS
AMONG KNEE OSTEOARTHRITIS PATIENTS IN
OUTPATIENT CLINIC, HOSPITAL UNIVERSITI
SAINS MALAYSIA**

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LIST OF ABBREVIATIONS

ACR	American College of Rheumatology
ADL	Activity of daily living
aOR	Adjusted Odds Ratio
BMI	Body mass index
CI	Confidence Interval
COPCORD	Community Oriented Program for the Control of Rheumatic Diseases
EULAR	European League against Rheumatism
FELDA	Federal Land Development Authority
HIV	Human Immunodeficiency Virus
HRPZ II	Hospital Raja Perempuan Zainab II
HUSM	Hospital Universiti Sains Malaysia
KRK	Klinik Rawatan Keluarga
ILAR	International League Against Rheumatism
IA	Intra articular
MLR	Multiple Linear Regression
NHANES	National Health and Nutrition Examination Survey
NSAIDs	Non steroidal anti inflammatory drugs
NCCAM	National Center for Complementary and Alternative medicine
NHIS	National Health Interview Survey
OA	Osteoarthritis
ROM	Range of movement
SD	Standard Deviation

SMD	Standardized mean difference
SLR	Simple Linear Regression
SPSS	Statistical Package for Social Science
TCM	Traditional and complementary medicine
TENS	Trans-cutaneous electrostimulation
USM	Universiti Sains Malaysia
WHO	World Health Organization
WOMAC	Western Ontario and McMaster Universities Arthritis Index

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ABSTRAK

PENGGUNAAN PERUBATAN TRADISIONAL DAN KOMPLEMEN SERTA FAKTOR-FAKTOR YANG BERKAITAN DI KALANGAN PESAKIT OSTEOARTHRITIS LUTUT DI KLINIK PESAKIT LUAR, HOSPITAL UNIVERSITI SAINS MALAYSIA

Pengenalan: Osteoarthritis adalah penyakit sendi kronik yang utama, terutamanya di kalangan golongan tua. Ia dilaporkan sebagai antara 10 penyakit utama di dunia yang mengakibatkan kesusahan dan kecacatan. Rawatan penyakit Osteoarthritis pada hari ini tidak mampu untuk menyembuhkannya, walaubagaimanapun ia boleh mengurangkan kesakitan, membantu fungsi sendi dan seterusnya meningkatkan kualiti hidup pesakit. Selain perubatan moden, terdapat sebilangan pesakit yang menggunakan kaedah perubatan tradisional dan komplemen (TCM) untuk merawat penyakit mereka. Di antara mereka, ada yang hanya bergantung kepada kaedah TCM dan ada juga yang menggabungkan kedua-dua kaedah perubatan moden dan juga TCM.

Walaupun TCM digunakan secara meluas, sebahagian produk TCM di pasaran tidak diketahui kualiti, kandungan dan keberkesanannya malah berisiko tercemar dengan bahan terlarang atau racun berjadual seperti steroid, hormon, antihistamin dan logam berat. Pesakit juga berisiko mengalami interaksi apabila ia digunakan bersama dengan ubatan lain.

Objektif: Objektif kajian ini dijalankan adalah untuk mengenal pasti peratusan pesakit Osteoarthritis lutut di klinik pesakit luar, Hospital Universiti Sains Malaysia (HUSM) yang

menggunakan kaedah tradisional dan komplemen untuk merawat penyakit Osteoarthritis. Kajian ini juga mengkaji faktor-faktor yang berkaitan dengan penggunaannya.

Metodologi: Sebuah kajian keratan rentas telah dijalankan yang melibatkan seramai 214 pesakit Osteoarthritis lutut yang mengunjungi klinik pesakit luar HUSM (Klinik Rawatan Keluarga) dari bulan May 2013 hingga Oktober 2013. Pemilihan secara persampelan mudah telah digunakan dalam kajian ini. Pesakit ditemuramah terlebih dahulu untuk mendapatkan data asas pesakit, sejarah penyakit dan juga penggunaan perubatan tradisional dan komplemen. Seterusnya pesakit diberikan 1 set soalan khusus iaitu 'WOMAC (Western Ontario and McMaster Universities Arthritis) Index' dalam versi bahasa Melayu untuk menilai tahap keterukan penyakit Osteoarthritis lutut mereka dari segi sakit, kekejangan dan juga kesusahan dalam aktiviti harian.

Keputusan: Hasil kajian ini mendapati peratusan pesakit yang menggunakan kaedah tradisional dan komplemen untuk merawat penyakit Osteoarthritis lutut adalah sebanyak 57.9%. Faktor yang berkaitan dengan penggunaan perubatan tradisional ini adalah faktor jantina iaitu lelaki (OR; 2.47, 95% CI: 1.28, 4.77), tempoh penyakit Osteoarthritis lutut (OR; 1.51, 95% CI: 1.03, 2.23) dan keterukan sakit lutut (OR; 2.57, 95% CI: 1.71, 3.86).

Kesimpulan: Peratusan penggunaan perubatan tradisional dan komplemen (TCM) untuk merawat penyakit Osteoarthritis lutut di kalangan populasi ini adalah tinggi. Para doktor disarankan agar peka dan mengenal pasti pesakit mereka yang mengamalkan kaedah ini agar perbincangan isu-isu berkaitan dan keputusan bersama boleh dilakukan.

ABSTRACT

Title: Use of Traditional and Complementary Medicine (TCM) and its associated factors among knee Osteoarthritis patient in outpatient clinic, HUSM.

Introduction: Osteoarthritis is the commonest arthritis worldwide especially in elderly. It ranks among the top ten causes of disability worldwide. The current management of Osteoarthritis does not provide definitive cure, however it was able to control pain, improved function and overall quality of life. Other than conventional treatment, some patients opted for traditional and complementary medicine (TCM) to treat the disease. Some of them use it alone however most of the patient combine both the conventional and TCM. Even though TCM is widely used, many of its marketed products were questionable in term of quality, efficacy, content and safety. There are many unregistered product which found to be contaminated with controlled drugs and poisons such as steroid, hormones, antihistamine and heavy metal which can cause a lot of unwanted effect and complication.

Objectives: To determine the proportion of knee Osteoarthritis patient at HUSM outpatient clinic who uses traditional and complementary medicine (TCM) for their knee Osteoarthritis and its associated factors.

Methodology: This study is a cross sectional study. 214 numbers of patients were involved in this survey. Convenience sampling method was applied to select participants who attended outpatient clinic in HUSM (Klinik Rawatan Keluarga) from May 2013 to October 2013. First, participants were interviewed to get the sociodemographic characteristics, clinical history and history of TCM use for knee osteoarthritis. After that, patients were given a questionnaire which is validated Malay version of Western Ontario and McMaster Universities Arthritis Index (WOMAC) to be self-administered. This questionnaire was used to assess the severity of knee osteoarthritis in term of pain, stiffness and disturbances in daily activity. The data was analyzed using the descriptive statistic and multiple logistic regressions.

Result: This study showed that the proportion of knee Osteoarthritis patient attended HUSM out-patient clinic that practice traditional and complementary medicine was 57.9%. Factors associated with TCM use in this study population was male (OR; 2.47, 95% CI: 1.28, 4.77), duration of knee Osteoarthritis (OR; 1.51, 95% CI: 1.03, 2.23) and severity of knee pain (OR; 2.57, 95% CI: 1.71, 3.86).

Conclusion: The proportion of TCM use for knee Osteoarthritis in this population study was high. Clinicians should aware of its high usage. They should identify patients by asking them regarding use of TCM so further discussion and shared decision can be undertaken.

CHAPTER 1

INTRODUCTION

1.1 Epidemiology of Osteoarthritis

Osteoarthritis (OA) is a progressive degenerative joint disease involving the cartilage and its encompassing tissue [1]. It is the commonest cause of arthritis worldwide and almost a universal problem in people aged over 65 years old [2]. Osteoarthritis has a major contribution to the burden of joint pain and is the most important musculoskeletal cause of pain and loss of joint function in elderly, largely due to knee and hip involvement.

Prevalence of OA varies broadly relying upon definition used, sex, age, the particular joints examined and the characteristics of the study population. The most widely utilized case definitions are clinical OA, radiographic OA and symptomatic OA. Clinical OA is easily diagnosed by the presence of symptoms in the history and sign on examination. It requires the vicinity of joint pain in addition to other features. The most set up gauges for the determination of clinical OA are the American College of Rheumatology (ACR) clinical criteria. These have been produced for the knee [3], hip [4] and hand [5]. For radiographic OA, the most common used classification was the Kellgren and Lawrence (K&L) score. It has been used by WHO as a reference score for its epidemiological study. It grades the severity from 0 to 4 related to appearance of osteophytes, joint space loss, sclerosis and cysts [6]. Not all individual with radiographic OA has the symptoms and disability, therefore it has the

highest reported prevalence. The other definition which is symptomatic OA is defined by the presence of pain, aching, or stiffness in a joint with radiographic features of OA.

An estimation by World Health Organization (WHO) shows symptomatic OA affects 18% of women and 9.6% of men age more than 60 years old [7]. Other estimation by Global Burden of Disease 2010 shows more than 250 million people suffered from knee OA alone worldwide. They found out the prevalence rising with age and peak at the age of 50 [8]. OA is more common among women than men and its incidence increments drastically around the time of menopause [9].

The prevalence of symptomatic knee OA among adult was lower compared to the radiographic knee OA. In Framingham study, the prevalence of symptomatic knee OA among subjects age more than 26 years old was 4.9% compared to the radiographic knee OA which was 19.2% [10]. While in the Johnston County study, among subjects age above 45 years old, the prevalence was 16.7% for symptomatic knee OA and 27.8% for radiographic knee OA [11]. Whereby in NHANES III it was reported as 12.1% of symptomatic knee OA as compared to 37% of radiographic knee OA among participants age more than 60 years old [10].

Beijing Osteoarthritis Study is a population-based study of elderly aged 60 years and above, which identical to the Framingham OA study. They found out 5.6% of men and 15% of women from the population suffered from symptomatic knee OA. Ladies in Beijing had a higher prevalence of symptomatic knee OA if contrasted with ladies of the same age in Framingham (prevalence ratio=1.43, 95% CI 1.16 to 1.75). However, the prevalence of knee OA among men in both studies was similar (prevalence ratio of 1.02 for symptomatic OA and 0.90 for radiographic OA). Genetic factors and heavier activity observed among Chinese would explain these differences [12].

A survey did in Asian region found that the prevalence of clinically diagnosed knee OA was range between 1.4% in urban Filipinos to 19.3% in rural part of Iran [13]. Physical and socioeconomic environment could be part of reason for this difference.

In our country, the data about prevalence of OA was come from the Community-Oriented Program for the Control of Rheumatic Diseases (COPCORD) studies. This research was initiated by International League Against Rheumatism (ILAR) and the World Health Organization (WHO). They found out 9.3% of adult Malaysians involved in the study had knee pain and more than half of those examined had clinical evidence of OA. The prevalence varies based on gender and ethnic groups. The prevalence increases with age and more common in women. It was 1.1% in Chinese women, 1.3% in Chinese men, 1.6% in Malay men, 2.6% in Indian men, 3.2% in Malay women and 5.6% in Indian women. However, these findings are likely to be underestimated, since they only included persons who complaining of current pain. Some more, not all subjects with knee pain attended the second phase for subsequent physical examination [14].

1.2 Diagnosis of Osteoarthritis

Osteoarthritis (OA) is frequently diagnosed by clinical impression from the history and physical findings. European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) have developed a diagnostic criteria which can be used as a guide [15]. Clinical features of OA depend on the severity and extent of the disease. However, symptoms may correlate poorly with radiological evidence of OA. For examples, patients may be asymptomatic but have radiological evidence of OA.

Symptoms of OA include the joint pain, joint stiffness after episode of inactivity, gait disturbance, clicking and grinding sensation on joint motion [15]. The most common

presenting complaint was the joint pain. It is usually insidious in onset with variable intensity throughout the day. The pain increased by joint use and impact and the pain relieved by rest. In patient with severe OA, they may be experience night pain which disturb sleep. Stiffness in

OA usually lasts only a few minutes and almost always less than 30 minutes in contrast to inflammatory arthritis such as rheumatoid arthritis. It usually occurs after period of inactivity, such as in the morning or when arising after sitting or lying. OA of knee may be associated with gait disturbance, increased muscle spasm and later disturb quality of life [15].

Signs of OA include altered in gait patterns (especially if it involved weight-bearing joints), joint swelling, joint tenderness, crepitus sensation, limitation of motion and joint deformity [14]. Long standing and severe OA may have loss of joint function with reduced motion as a result of effusion or periarticular soft tissue contractures. Any of the peripheral joints with OA may be presented with deformity. Among the common joint deformity for knee OA was the varus deformity [15].

The American College of Rheumatology (ACR) has developed diagnostic criteria for osteoarthritis at various sites, including the knee. Diagnostic criteria for osteoarthritis of the knee can be based either on clinical and laboratory, clinical and radiographic or clinical alone with different sensitivity and specificity. Clinically knee OA is diagnosed as knee pain for most days of the prior month and at least three of the following criteria: patient age more than 50 years old, morning stiffness lasting less than 30 minutes, crepitus on motion, bony tenderness, bony enlargement and no palpable warmth. This criteria is widely accepted as the standard diagnostic criteria for knee OA with 95% sensitivity and 69% specificity if presented three of listed criteria and 84% sensitivity and 89% specificity if four criteria [3]. A table below illustrates the ACR recommended diagnostic criteria of knee OA [15].

<div>Diagnosis</div> <div>Criteria</div>	Clinical and laboratory	Clinical and radiographic	Clinical only	
Must have	Knee pain + At least 5 of 9 of the following	Knee pain + Osteophytes on x-ray + At least 1 of 3 of the following	Knee pain + At least 3 of 6 of the following	
1	Age >50 years	Age >50 years	Age >50 years	
2	Stiffness <30 min	Stiffness <30 min	Stiffness <30 min	
3	Crepitus	Crepitus	Crepitus	
4	Bony tenderness		Bony tenderness	
5	Bony enlargement		Bony enlargement	
6	No palpable warmth		No palpable warmth	
7	ESR <40			
8	RF <1: 40			
9	SF OA			
Sensitivity	92%	91%	95%	84%
Specificity	75%	86%	69% (if 3/6)	89% (if 4/6)

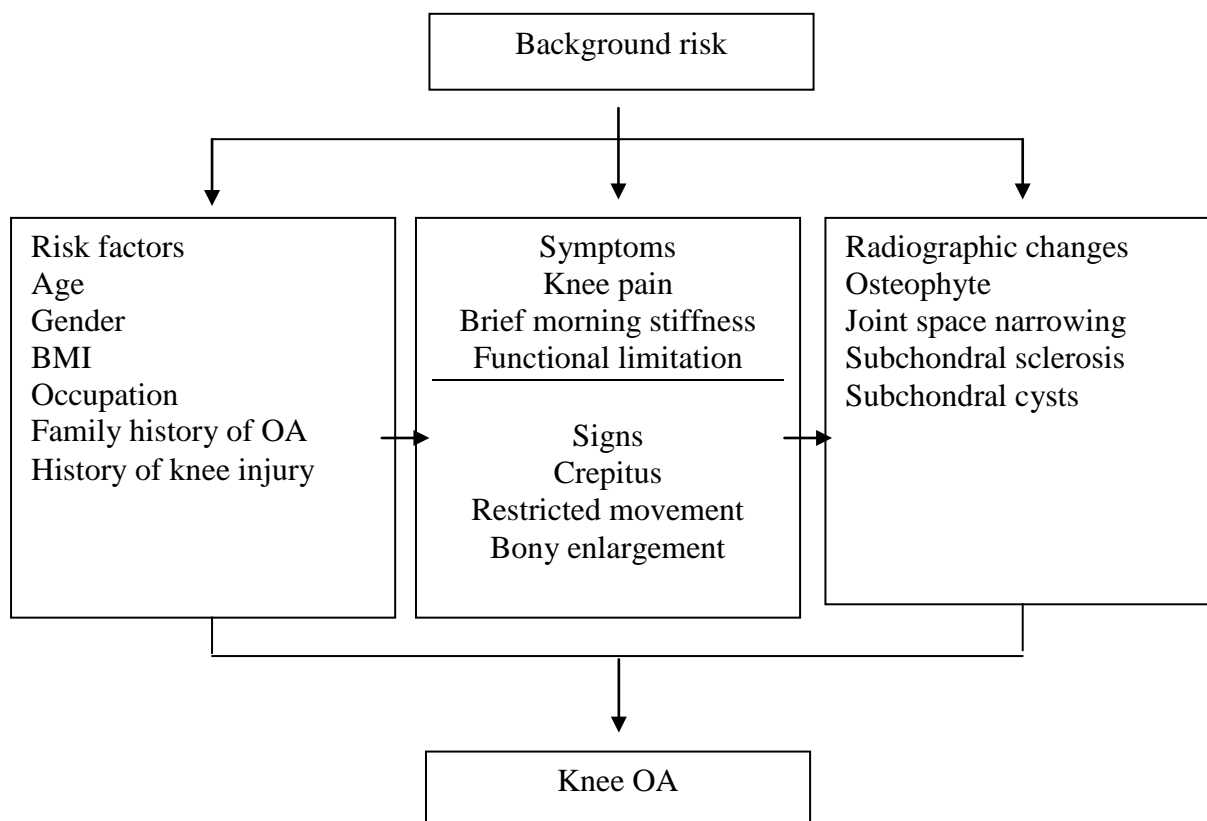
ESR=erythrocyte sedimentation rate RF=rheumatoid factor

SF OA=synovial fluid signs of OA (clear, viscous, or white blood cell count <2,000/mm³)

Other than ACR criteria, European League Against Rheumatism (EULAR) also had developed its own recommendation for diagnosis of knee OA [16].

According to the EULAR, the diagnosis of knee OA can be made based on the background risk (the population prevalence of knee OA), the patient's risk factors for OA (eg. Age 50 years old and above, female gender, higher BMI), their symptoms (persistent knee pain and functional limitation) and an adequate physical examination (crepitus or restricted movement). Plain radiographs act only an adjunct tool for the purposes of diagnosis.

The figure below describes the recommendation [16].



1.3 Management of Osteoarthritis

Management of Osteoarthritis (OA) involves non-pharmacological and pharmacological approaches. The goals of treatment include symptom alleviation, minimize disability, improvement in functional status as well as overall quality of life [15].

Non-Pharmacological Treatment

The recommended non-pharmacological part of management of OA includes patient education, lifestyle modification (weight reduction and physical activity), physiotherapy (transcutaneous electrostimulation, thermotherapy and therapeutic ultrasound) and occupational therapy [15].

Patient education

Patient education is always a crucial part in managing chronic illnesses include the OA. The main target is to encourage a positive attitude towards the illness. The education should include information of the diagnosis, nature of the illness, therapeutic options and the importance of patient participation as part of the disease management. However it has to be tailored to each individual's functional status, needs and reasonable target [17, 18]. It was found that patients will cope better and reported less pain if they understand the disease [19].

Lifestyle modification

In knee OA, the lifestyle changes focus on physical activity or exercise and weight reduction. Weight reduction was found to be effective in pain reduction and improvement of function especially in obese patient with knee OA [20].

Exercise was found to be effective in reducing pain in knee OA. In systematic review of 54 RCT from Cochrane database, they found out land based exercise is effective in reducing pain immediately after treatment (Standardized mean difference (SMD)-0.49, 95% (CI) -0.39 to -0.59), improving physical function (SMD -0.52, 95% CI - 0.39 to -0.64) and improved quality of life (SMD 0.28, 95% CI 0.15 to 0.40). This land-based exercise program which consisting of functional training, traditional muscle strengthening and aerobic fitness program was found to give benefit in term of reduced knee pain and improved in physical function among people with knee OA. The effect is sustained for at least two to six months after cessation of formal treatment [21].

Physiotherapy

Physiotherapy can improve muscle strength, balance, coordination and joint mobility. It consists of transcutaneous electrostimulation (TENS), thermotherapy and therapeutic ultrasound. Transcutaneous electrostimulation (TENS) and thermotherapy were recommended by ACR as part of management of knee OA [22]. However, for therapeutic ultrasound, even though it was found to be beneficial in pain control and improved function, its effectiveness was inconclusive due to low quality of evidence [23].

Occupational therapy is another crucial part of non-pharmacological treatment. Activity modification in performing ADL such as use of walking stick on the opposite hand of the affected knee, to climb stairs using railing of the stairs, to bathe or cook in a certain position, to avoid high heeled shoes and to avoid performing activity in squatting position were found to improve pain (SMD= -3.21, 95 % CI -3.45 to -0.70) at 6 weeks [24].

Appliance of Orthoses such as walking shoes with neutral or laterally wedge insole was found by Cochrane review as lack of an effect in reducing pain, stiffness and function [25]. Another modality which is widely used for knee OA was brace.

However it was also failed to shows any clinical or statistics evidence to reduce pain, improve function or quality of life [25].

Pharmacological Treatment

Pharmacological treatments are available in the form of oral, intra-articular and topical. At present, no pharmacologic treatment which found can prevent the progression of joint damage due to OA.

Oral treatment suggested incorporates simple analgesics (eg. Paracetamol), weak opioid analgesics (eg. Tramadol), analgesics with anti-inflammatory properties (eg. Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Cyclo-oxygenase-2 (COX-2) Inhibitors) and nutraceutical (eg. glucosamine, chondroitin, diacerein) [15]. Each of the oral treatment mentioned above was found to be effective in treating OA. In RCT, Paracetamol, Tramadol and NSAIDs including COX-2 inhibitors on regular basis were found more efficacious than placebo in reduction overall pain and improving stiffness and function [26-29].

In National guidelines management of Osteoarthritis, Paracetamol should be used as first line analgesic in mild to moderate pain before stepped-up the treatment if persistent symptoms [15]. It is safe and well tolerated [26, 27]. However in recent NICE updates, it found lack of effectiveness of Paracetamol in the management of OA compared to previous findings. But until they come out with a full review of pharmacological management of OA, it is still recommended to offer Paracetamol for pain relief in addition to core treatment which is non pharmacological. They also recommended used of topical NSAIDs ahead of oral NSAIDs, cyclo-oxygenase 2(COX-2) inhibitors or opioids [30].

Tramadol even though has no major adverse event, many patient discontinue the medication due to common side effect such as dizziness, nausea and constipation which limit its usefulness [28]. NSAIDs including COX-2 inhibitors were not recommended for long-term use due to potential of gastrointestinal, cardiovascular and renal adverse effect which also limited its usefulness [29].

In National guidelines management of Osteoarthritis, used of Glucosamine, Chondroitin and Diacerein have been considered as part of pharmacological treatment under nutraceutical group [15]. A review of 5 systematic reviews indicates evidence that Glucosamine sulphate shows some clinical effectiveness in the treatment of OA of the knee in term of short term pain control. In two studies of glucosamine sulphate, both funded by the manufacturer (Rotta, Italy) of an oral powder product, the need for surgery which is knee arthroplasty was reduced from 14.5% to 6.3% at 8 years follow-up. However, for non- Rotta preparations of glucosamine, it was inconclusive to support a clinical effect [31-33].

For Chondroitin Sulfate, a Cochrane review of 43 trials involving 9110 patients shows that it was better than placebo in improving pain but for short term duration only. However most trials are of low quality and recommended for high quality studies to further explore its effectiveness for OA [34]. Its effectiveness as a structure modifier or biological agent for OA was not consistent. In term of safety profiles, both were well-tolerated and safe [31, 32, 34].

Diacerein is proven to be effective in pain reduction however its benefit was minimal [35]. Generally it is safe but significant adverse effect observed was gastrointestinal symptoms which is diarrhoea [35].

For intra-articular (IA) treatment, injection of IA corticosteroid has offered relief of pain but for short-term only without improvement in function [36]. Another IA treatment was Hyaluronic acid (HA) intra-articular injection, or commonly called visco-supplementation.