OUTCOME OF NON-OPERATIVE TREATMENT OF PATIENTS WITH PRIMARY OSTEOARTHRITIS OF THE KNEE AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

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SM/PGORT/07/13

"Thesis submitted in partial fulfilment of the requirement for the award of degree of Master of Medicine in Orthopaedic surgery, Moi University"

DECLARATION

Declaration by Candidate

"This thesis is personal work and has not been presented for a degree to any other University or Institution".

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DEDICATION

This work is dedicated to my parents Mr and Mrs Evans Mwaura who did their level best to ensure that I got the best education despite many odds.

Also to thank my wife Stella Kiptoo-Hinga and daughters Natasha Mbaire and Tiffany Jepkoech for their unwavering support during this process.

ABSTRACT

Background: Primary osteoarthritis (OA) is a chronic disorder of synovial joints in which there is progressive softening and damage of articular cartilage and ultimately joint destruction. In Kenya,70% of OA cases are due to knee OA. Treatment is non-operative for mild to moderate cases and surgical for severe cases. Few studies have been done locally to determine non-operative treatment methods and their outcome. The study aims to address this gap.

Objectives: To determine outcome of non-operative treatment of primary OA of the knee at Moi Teaching and Referral Hospital (MTRH).

Methods: A hospital based descriptive prospective study was carried out at MTRH orthopaedic clinic involving patients managed for primary OA of the knee between 1st January 2017 to 30th June 2018. Those included were all new adult patients with primary OA of the knee. Patients with secondary OA of the knee and rheumatoid arthritis were excluded. Study participants enrolled were 72 but 4 were lost to subsequent follow up. Information on osteoarthritic indicators of pain, stiffness and limitation in function was collected using radiographs, questionnaires and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) at 0, 3 and 6 months. Non-operative treatment types and changes in symptomatology with different prescribed treatment methods in the clinic was then followed. Collected data was analysed and presented in form of figures, tables and graphs.

Results: Median age of the respondents was 64 years (IQR 56,69years). Majority were female (80.6%). Most respondents were employed in the informal sector (68. 1%).Most respondents were of normal body mass index (41.7%). Hypertension was the most common co-morbidity seen in 12.5% of all patients. Obesity was present in 23.7% of cases. The most affected knee was right in 45.8% of the respondents, followed by left (33.4%) then bilateral (20.8%). Most respondents had duration of symptoms of less than 5 years (82.0%). A total of 69 patients had abnormal x-ray findings. Treatment administered consisted of lifestyle modification in all patients, non-steroidal anti-inflammatory drugs (NSAIDS) in 94.1% of respondents, opioids (2.9%) and steroids (2.9%). Glucosamine/chondroitin sulphate was given as an adjunct treatment in 49.9% of respondents. Other adjunct treatments given were knee bracing and physiotherapy. Most patients improved over the 6 months of the study. Only 19.4% of patients had mild symptoms (WOMAC score 0-32 points) at the beginning of the study which increased to 85.3% at 3 months, then dropped to 67.6% at 6 months. Moderate symptoms (WOMAC score 33-65 points) were observed in 75.0% of respondents at the beginning of the study, which dropped to 13.1% at 3 months and 30.1% of respondents at the end of the study. Severe symptoms (WOMAC score greater than 65 points) were observed in 5.6% of respondents at the beginning of the study and 1.5% of respondents at 3 and 6 months. There was no significant association between OA of the knee with BMI and hypertension (p-value 0.881 and 0.335 respectively)

Conclusion: Primary OA of the knee had high occurrence in elderly female patients at MTRH, with good treatment outcome after 6 months of combined non-operative treatment methods, with NSAIDS and glucosamine/chondroitin sulphate being the main drugs used.

Recommendation: Standard protocols for non-operative treatment of primary knee OA should include NSAIDS. Control and preventive measures against the modifiable risk factors for primary OA of the knee should be encouraged. Further research on long term outcome of primary OA of the knee.

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ABBREVIATIONS AND ACRONYMS

AA	ARACHIDONIC ACID
AAOS	AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS
ACR	AMERICAN COLLEGE OF RHEUMATOLOGY
AHRQ	AGENCY FOR HEALTHCARE RESEARCH AND QUALITY
BMI	BODY MASS INDEX
BPH	BENIGN PROSTATIC HYPERTROPHY
CBC	COMPLETE BLOOD COUNT
COX 1	CYCLOOXYGENASE 1
COX 2 SELECTIVE	CYCLOOXYGENASE 2 SELECTIVE
CRP	C-REACTIVE PROTEIN
CSDH	CHRONIC SUBDURAL HAEMATOMA
DM	DIABETES MELLITUS
DMARDS	DISEASE MODIFYING ANTI-RHEUMATIC DRUGS
ESR	ERYTHROCYTE SEDIMENTATION RATE
I.L	INTERLEUKIN
IREC	INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE
KL GRADE	KELLGREN LAWRENCE GRADE
MRI	MAGNETIC RESONANCE IMAGING

MTRH	MOI TEACHING AND REFERRAL HOSPITAL
NSAIDS	NON STEROIDAL ANTI-INFLAMMATORY DRUGS
O.A	OSTEOARTHRITIS
OARSI	OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL
ORIF	OPEN REDUCTION AND INTERNAL FIXATION
PG	PROSTAGLANDIN
RCT	RANDOMISED CLINICAL TRIALS
RA	RHEUMATOID ARTHRITIS
SLE	SYSTEMIC LUPUS ERTHROMATOSUS
SPSS	STATISTICAL PACKAGE FOR THE SOCIAL SCIENCES
SR	SYSTEMIC REVIEWS
TENS	TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION
TXA2	THROMBOXANE A2
WOMAC	THE WESTERN ONTARIO AND MCMASTER UNIVERSITIES ARTHRITIS INDEX

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Lastly, I wish to express my unreserved thanks to my family for their tireless support and motivation.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background information

Osteoarthritis, also known as degenerative arthritis or degenerative joint disease or osteoarthrosis, is a group of mechanical abnormalities involving degradation of joints including articular cartilage and subchondral bone (Solomon et al., 2010).

It involves progressive softening and disintegration of articular cartilage accompanied by growth of osteophytes, cyst formation, and subchondral sclerosis (Vaishya et al., 2016).

Osteoarthritis is rising in the world's aging populations; it is the sixth among leading causes of years lost because of disability globally. Up to 3% disability globally is due to Osteoarthritis – 10% of men and 18% of women over the age of 60 (Ceme, 2008).

The annual incidence of symptomatic knee O.A is 240/100,000 persons per year, which is higher than hip O.A at 88/100,000 persons per year (Watts & Karadsheh, 2018).

By the age of 65, approximately 80% of the United States of America population is affected by osteoarthritis. Of the total persons affected, osteoarthritis of the knee constitutes 80% of the total disease burden (Vaishya et al., 2016).

In Africa, prevalence of osteoarthritis is 55.1% of total arthritis cases of which 33.1% is osteoarthritis of the knee (Usenbo et al., 2015).

In Kenya, 39.77% of patients presenting with musculoskeletal conditions are diagnosed with Osteoarthritis. Of these, osteoarthritis of the knee constitutes 70% (Nour et al., 2013). Majority are female (86%).

Although there is no known cure for OA, treatment designed for the individual patient can reduce pain, improve joint mobility, and limit functional impairment. Non-operative management is useful in patients with KL-Grade 1-3 osteoarthritis, whereas surgical options including joint replacement surgery is usually employed in KL-Grade 4 disease (Behzad, 2011).

Joint replacement surgery in Kenya is expensive and beyond the reach of many people with an average cost of Ksh 500,000/= required to replace both knees at MTRH.

1.2 Problem statement

Primary osteoarthritis of the knee is the most common form of arthritis disorder especially in Kenya's aging society constituting 70% of all osteoarthritis cases. (Nour et al., 2013).

As a result, there is significant pain, deformity and loss of function in the knee of the affected person which leads to disability of the affected person. This further leads to inactivity and subsequent loss of livelihood for the affected person and his/her dependants due to inability to work.

There has been an increase in number of patients with primary OA of the knee seen at MTRH. However, their non-operative treatment is not standardized and there is no data on their outcomes. This study aims to bridge this gap.

1.3 Justification

It is hoped that the information obtained in this study will help in future management of patients with primary osteoarthritis of the knee to improve outcomes.

Although there is no known cure for osteoarthritis, effective treatment regimens designed for patients will reduce pain, improve joint mobility and limit functional impairment.

As there is no local data on these patients the study will seek to create new information on this group of patients at MTRH in Eldoret.

Additionally, this study may act as a baseline for development of other related studies.

1.4 Research Question

What is the outcome of non-operative treatment of patients with primary osteoarthritis of the knee at Moi Teaching and Referral Hospital (MTRH)?

1.5 Objectives

1.51. Broad Objective.

To determine outcome of non-operative treatment of patients with primary osteoarthritis of the knee at Moi Teaching and Referral Hospital.

1.52. Specific Objectives

1. To determine the demographic characteristics of patients with primary osteoarthritis of the knee at MTRH
2. To describe select co-morbidities in patients with primary osteoarthritis of the knee at MTRH.
3. To determine the types of non-operative methods used in treatment of primary osteoarthritis of the knee at MTRH
4. To determine the treatment outcome of non-operative methods used in treatment of primary osteoarthritis of the knee at MTRH using the WOMAC index for a study duration of 6 months.

CHAPTER TWO

2.0. LITERATURE REVIEW

2.1. Introduction

Osteoarthritis is a chronic disorder of synovial joints in which there is progressive softening and disintegration of articular cartilage accompanied by the growth of osteophytes (Hansen & Lambert, 2005).

Treatment designed for osteoarthritis aims at reducing pain, improving joint mobility, and limiting functional impairment. It can be achieved by operative and non-operative means. Non-operative treatment of OA is useful for patients with Kellgren-Lawrence grade 1–3, which are early stages of OA. However, in advanced stages of OA (Kellgren-Lawrence grade 4), surgical treatment is needed as definitive treatment (Vaishya et al., 2016).

2.1.1 Anatomy

The knee joint is located between the thigh and the leg. It is a complex joint formed by interaction between four main bones i.e. femur, tibia, fibula and patella, which interact with one another to form three distinct joints which constitute the knee joint (El-Din, 1981). These are:

1. Superior tibiofibular joint
2. Patellofemoral joint
3. Tibiofemoral joint

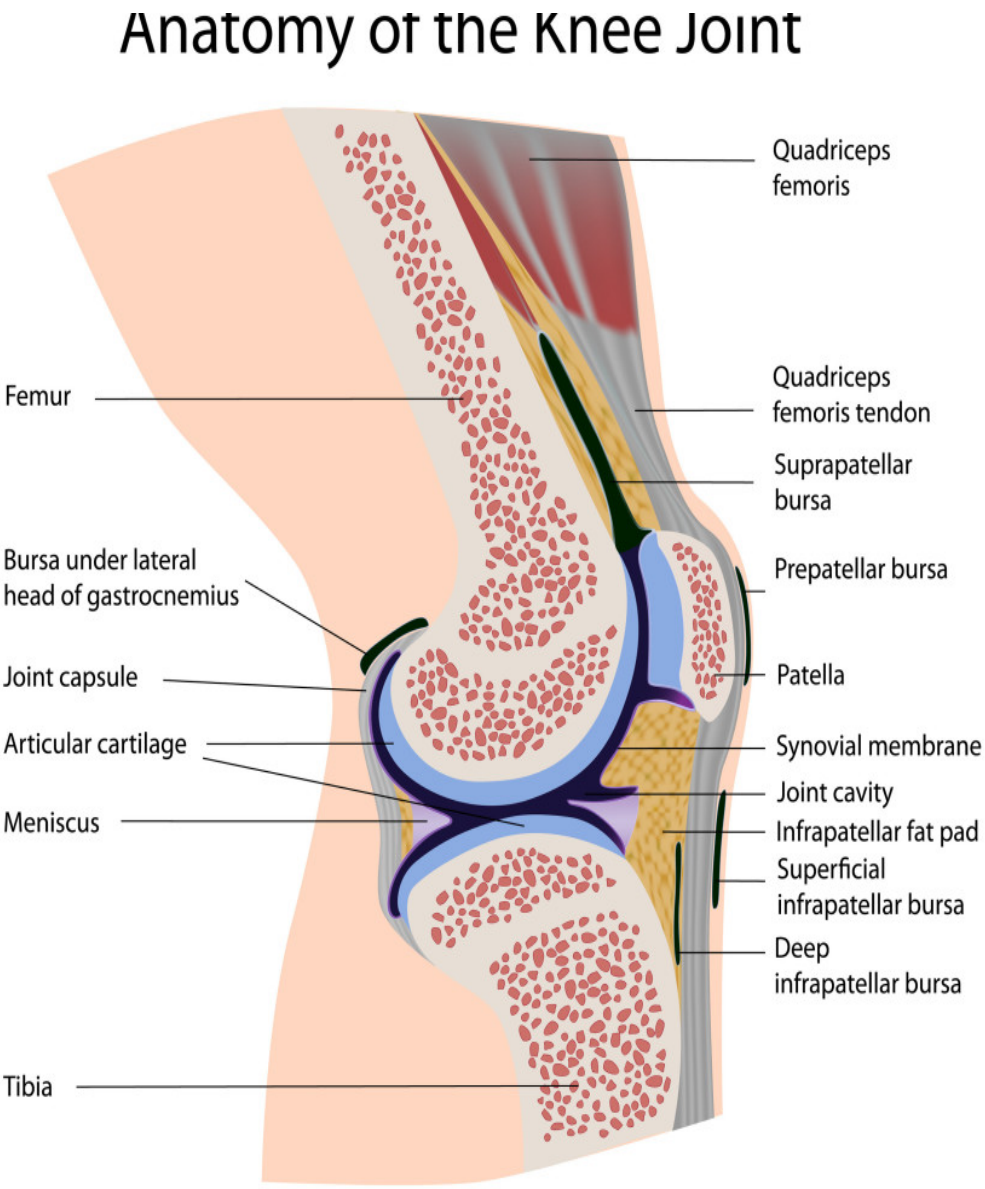


Figure 1: Anatomy knee joint (Anatomy Research Foundation, ARF, 2002).

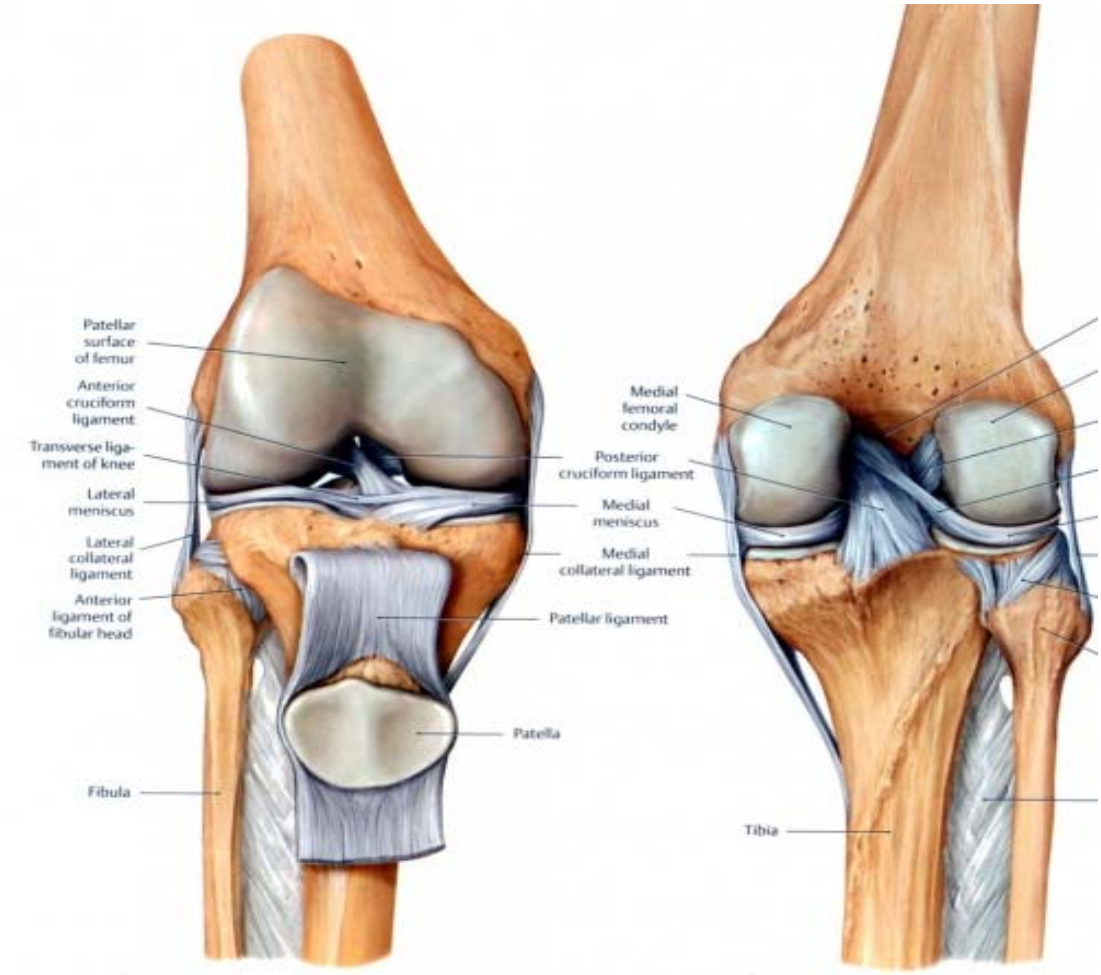


Figure 2: Anatomy of the knee joint (Agur & Dalley, 2005).

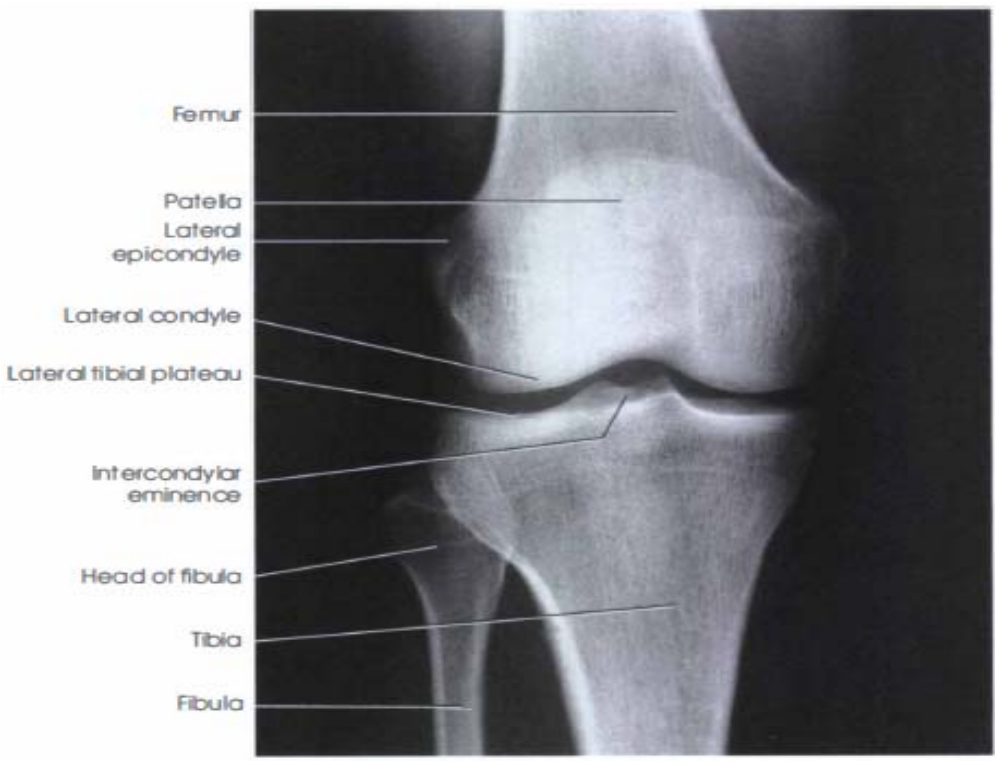


Figure 3: X-ray of the knee joint - AP view (Watts & Karadsheh, 2018).

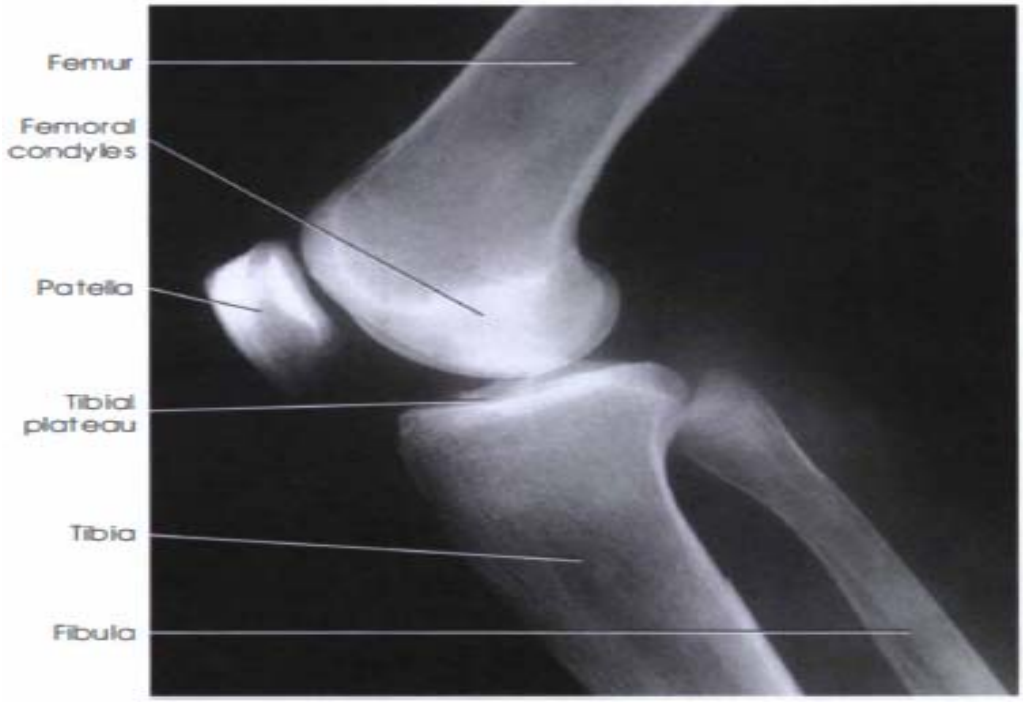


Figure 4: X-ray of the knee joint - lateral view (Watts & Karadsheh, 2018).

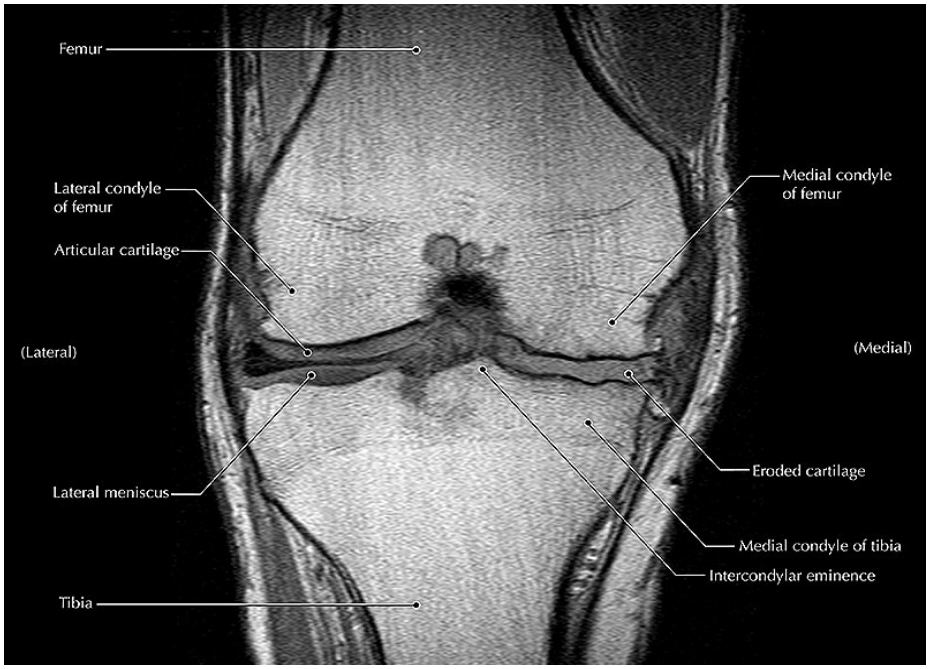


Figure 5: MRI imaging of the knee joint. Coronal view (Sharma et al., 2014).

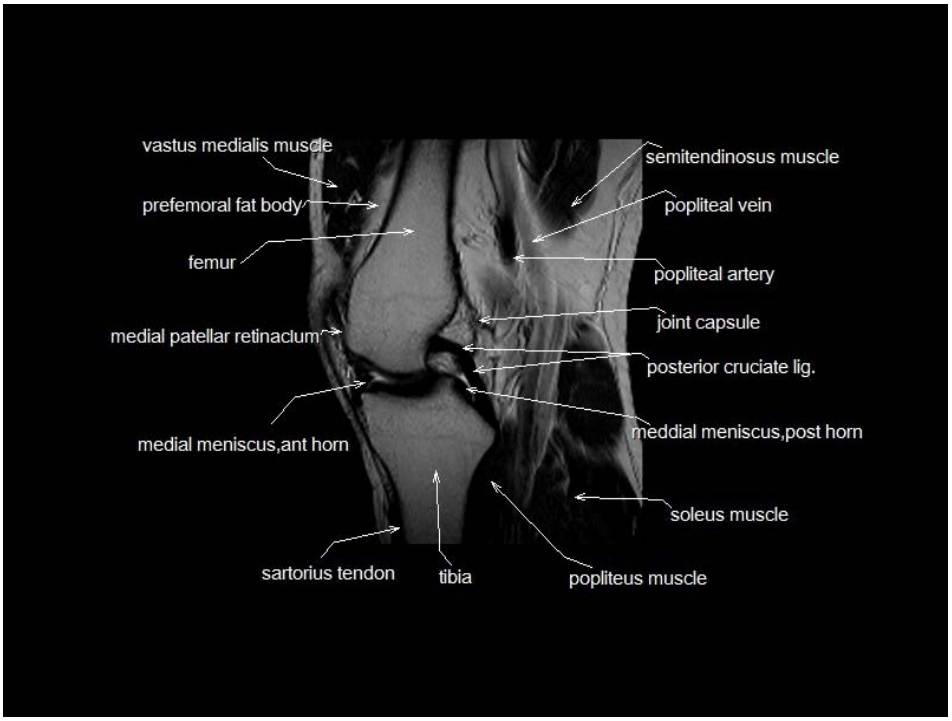


Figure 6: MRI imaging of the knee joint. Sagittal view (Sharma et al., 2014)

2.1.2 Background of osteoarthritis of the knee

Osteoarthritis (OA) a common disease of aged population and one of the leading causes of disability. Incidence of knee OA is rising by increasing average age of general population. Age, weight, trauma to joint due to repetitive movements in particular squatting and kneeling are common risk factors of knee OA (King'ori & Gakuu, 2010).

The economic costs of OA are high, including those related to treatment, for those individuals and their families who must adapt their lives and homes to the disease, and those due to lost work productivity (Dieppe, 1995).

Patients with OA are at a higher risk of death compared with the general population. History of diabetes, cancer, or cardiovascular disease and the presence of walking disability are major risk factors (Krishna & Lane, 2011).

Despite its severe consequences, however most patients with knee OA can be managed in the community and primary care (Buttgereit et al., 2014).

2.2 Epidemiology

The annual incidence of knee osteoarthritis is 240/100,000 persons per year. This is much higher than hip OA whose incidence is 88/100,000 persons per year (Watts & Karadsheh, 2018).

In a study of 763 patients in Kenya, 39.77% of patients with musculoskeletal symptoms were found to be suffering from osteoarthritis. Of these, osteoarthritis of the knee constituted 70% of the patients (Oyoo, 2004). This compared well to India studies where prevalence of O.A was between 22-39% with O.A of the knee contributing nearly 80% of the total O.A burden (Vaishya et al., 2016).

Another study in Kenya on 201 patients by Nour et al. (2013) established that 77% of total osteoarthritis cases were due to knee OA, of which 86% were women with a median age of 62.1 years. Hence a high prevalence in Kenya, though the study was a hospital based study.

Prevalence of knee OA in men is lower compared with women especially postmenopausal women (Agency for healthcare research and quality, AHRQ, 2002).

The prevalence of radiographic knee OA has been investigated in 2282 elderly Japanese people aged ≥ 60 years (817 men and 1,465 women) living in urban regions. There was a high prevalence of radiographic Knee OA (Behzad, 2011).

The prevalence of pain in the knee was age-dependent in women, but not in men. Symptomatic knee OA was common among the general adult population especially in women of older age groups.

In a cross-sectional study of 7 communities in Greece, symptomatic knee OA was observed in 6% (95% CI 5.6-6). The prevalence rate was significantly higher among women than in men and increased significantly with age. Symptomatic knee OA was significantly more common in rural compared to urban and suburban populations. Logistic regression analysis showed a significant association of female sex and age ≥50 years with all sites of OA. In addition, obesity and low level of education were associated with knee OA. Knee symptoms, radiographic knee OA, symptomatic knee OA, and severe radiographic knee OA were calculated in 3018 participants (33%) of African Americans (38% men) (Behzad, 2011).

Table 1: Distribution of musculoskeletal diseases in Kenya (Oyoo, 2004).

Disease	Number	Percentage %
Osteoarthritis	305	39.77
Rheumatoid arthritis	174	22.69
Soft tissue Rheumatism	109	14.21
Low back ache	80	10.23
Spondyloarthropathies	24	3.13
Gout	27	3.52
Osteoporosis	12	1.56
Others	32	4.89
Total	**763**	**100**

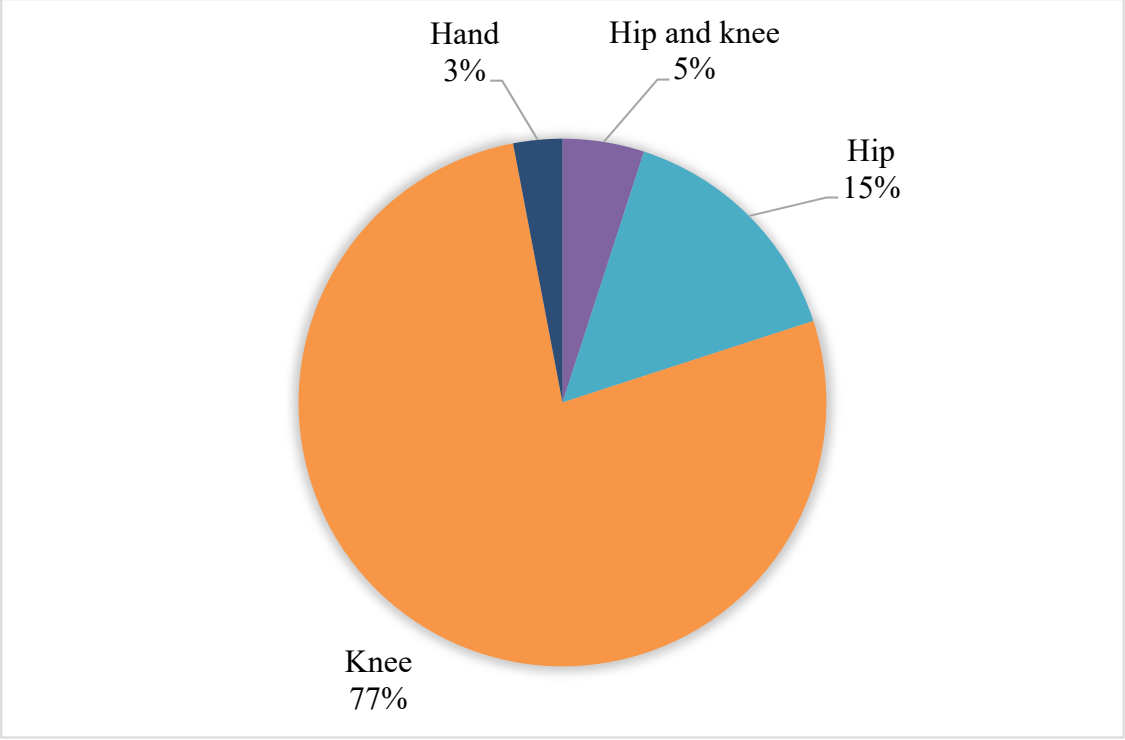


Figure 7: Distribution of joint diseases in 201 patients with OA (Nour et al., 2013).

2.3 Aetiology and risk factors of OA.

OA has multifactorial aetiologies, which occurs due to interplay between systemic and local factors.

Osteoarthritis affects all ages but is more prevalent in the elderly female population due to oestrogen deficiency. An international Irish study by French et al. (2015) published in the European Journal of Public health, Vol 26,2015 established a prevalence of 76% in females and 24% in male persons.

Sports participation, injury to the joint, obesity, and genetic susceptibility predispose adolescent athletes to the development of premature osteoarthritis. Previous knee trauma increases the risk of knee OA 3.86 times (Solomon et al., 2010).

Old age, female gender, overweight and obesity, knee injury, repetitive use of joints, bone density, muscle weakness, and joint laxity all play roles in the development of joint OA.

Female sex, lower educational levels, obesity, and poor muscular strength are associated with symptomatic disease and subsequent disability.

Smoking also contributes to osteoarthritis due to interference with blood supply to the joints and impairment of the body's repair mechanism and wound healing. A study by Dube (2016) established a prevalence of 6.2% of patients with primary osteoarthritis as smokers. Studies by Chin and Mehta (2008) and studies by Buckwalter et al. (2001) also determined positive association between smoking and primary osteoarthritis of the knee

On the other hand, new research has shown that rather than directly causing OA, aging changes in the musculoskeletal system contribute to the development of OA by making the joint more susceptible to the effects of other OA risk factors that include abnormal biomechanics, joint injury, genetics, and obesity (Loeser, 2010).

Table 2: Risk factors of knee osteoarthritis

Systemic risk factors	**Local risk factors**
Age	Obesity
Genetic susceptibility	Joint mechanics – alignment, proprioception, laxity.
Oestrogen deficiency	Muscle weakness
Smoking	Occupational stress
Race/Ethnicity	Physical activity
Gender	Knee injury
Metabolic syndrome	

2.4 Pathophysiology

The development of OA is dependent on interactions between several factors and so this process may be considered the product of an interplay between systemic and local factors.

This progressive and disabling disease can result from a combination of risk factors, including advancing age, genetics, trauma, knee mal-alignment, increased biomechanical loading of joints through obesity, augmented bone density and an imbalance in physiological processes (Lewis et al., 1999).

There is now a growing body of evidence that obesity is a complex syndrome in which an abnormal activation of neuroendocrine and pro-inflammatory pathways leads to an

altered control of food intake, fat expansion and metabolic changes. Activated white adipose tissue increases the synthesis of pro-inflammatory cytokines, such as IL-6, IL-1, IL-8, TNF alpha, IL-18, but decreases the regulatory cytokines, such as IL-10. This observation supports the link between obesity and OA. The obesity gene and its product leptin may have important implications for the onset and progression of OA (Hassanali, 2011). However, leptin can be also produced by osteoblasts and chondrocytes cells and local production of this substance may be of great importance. Significant levels of leptin were observed in the cartilage and osteophytes of people with OA, whereas few chondrocytes produced leptin in the cartilage of healthy people. Leptin was found in synovial fluids of OA joints which was correlated with BMI.

Cytokines, biomechanical factors, and proteolytic enzymes lead to variable degrees of synovial inflammatory process which up-regulate metalloproteinases and blunt chondrocyte compensatory synthesis pathways required to restore the integrity of the degraded matrix.

A cascade of changes in joint structure start from subchondral bone expansion, bone marrow lesions, meniscal tears and extrusion, to cartilage defects, which ultimately may lead to cartilage loss and radiographic osteoarthritis at late stage. Considerable evidence indicates that the menisci, ligaments, periarticular muscles and the joint capsule are also involved in the OA process.

Table 3: Articular cartilage changes in aging vs Osteoarthritis

	Aging	**Osteoarthritis**
Water content	Decreased	Increased
Collagen	Same	Disorganised
Proteoglycan content	Decreased	Decreased
Proteoglycan synthesis	Same	Increased
Chondrocyte size	Increased	Same
Chondrocyte number	Decreased	Same
Modulus of elasticity	Increased	Decreased

2.5 Grading of osteoarthritis of the knee

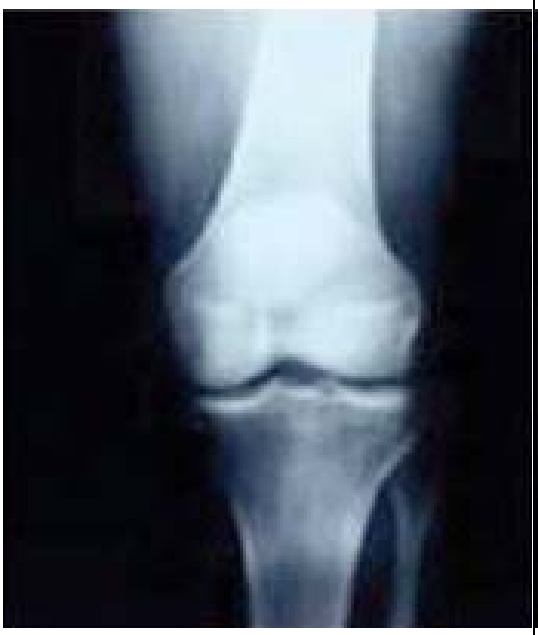
Kellgren–Lawrence (KL) grading system for knee OA is the most commonly used grading system and is based on a weight-bearing anteroposterior (AP) radiograph of both knees. The higher grades indicate more severe signs of OA and need for surgical intervention (Vaishya et al., 2016).

It is the most widely used grading combining x-ray characteristics of the affected bone and the size of the joint space.

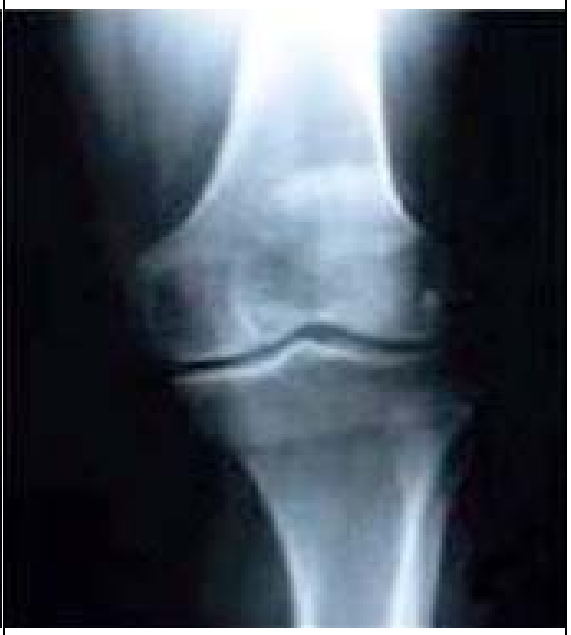
The main shortcomings of the grading are that it characterises progression of osteoarthritis as a linear process and also combines osteophytes and joint space narrowing measurements to come up with a grade, which in itself is erroneous as the changes can occur independently of each other (Marks, 2015).

Table 4: Kellgren – Lawrence Grading of Osteoarthritis (Vaishya et al., 2016)

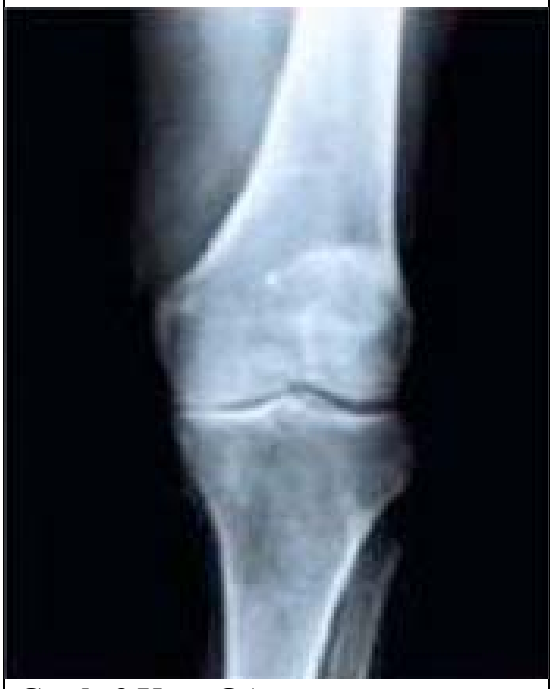
Grade	Findings
0	Normal, no findings
1	Questionable presence of osteophytes or joint space narrowing or both
2	Definite presence of osteophytes with possible joint space narrowing or definite mild joint space narrowing
3	Definite moderate joint space narrowing (at least 50%) osteophytes usually present, cysts/sclerosis may be present
4	Severe joint space narrowing with subchondral bone sclerosis and possible deformity of bone ends



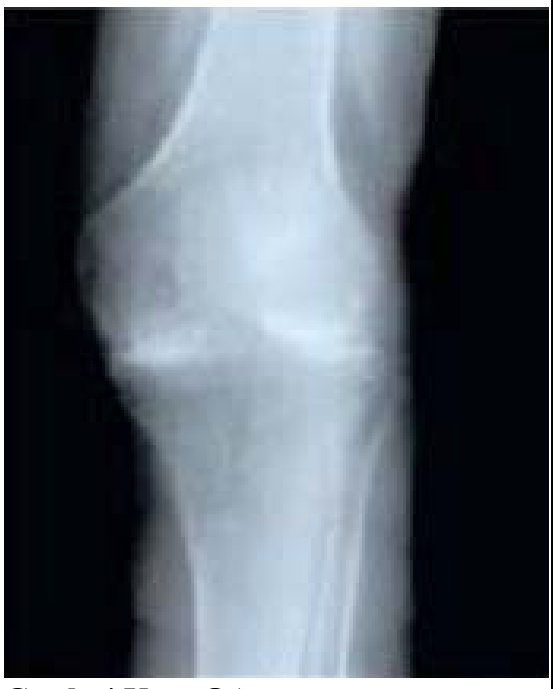
Grade I Knee OA



Grade 2 Knee OA



Grade 3 Knee OA



Grade 4 Knee OA

Figure 8: Radiological Grading of Knee OA (Watts & Karadsheh, 2018).

2.6. Clinical features

Persistent knee pain, limited morning stiffness, and reduced function are the three symptoms that are recommended for the diagnosis of knee OA (Vaishya et al., 2016). In addition, crepitus, restriction of joint movement and bony enlargement are also very useful for diagnosis of knee OA.

Pain is the most common symptom in knee OA, a leading cause of chronic disability, and a major source of the disability attributable to OA. Pain severity ranges from barely perceptible to immobilizing. Pain, in knee OA typically exacerbates by activity and relieves by rest. It may also be accompanied by swelling of the joint.

In the presence of the above six symptoms and signs the probability of having radiographic knee OA increases to 99%.

In advanced cases synovitis may appear and leads to pain at rest or night. Short duration of stiffness less than 30 minutes may be seen in OA patients in the morning or following periods of inactivity.

Tenderness to palpation of involved joints may be evident in physical examination. Joint effusions may be present, which typically exhibit a mild pleocytosis, normal viscosity, and modestly elevated protein. Crepitus during joint motion or walking is a common. Limitation of range of motion are all common signs of OA of the knee. These include lack of full knee extension and lack of full knee flexion (Watts & Karadsheh, 2018).

In advanced cases, mal-alignment may be apparent (genu varus or genu valgus) (Hassanali, 2011).

Table 5: Clinical presentation of Osteoarthritis of the knee

History	Symptoms	Physical Examination
1. Age – mainly elderly 2. Co-morbidities 3. Functional activity 4. Pattern of involvement 5. Duration of symptoms	1.Function limiting knee pain 2.Pain at night or at rest 3.Activity induced knee swelling 4.Knee stiffness 5.Mechanical symptoms – instability, locking and catching sensation.	1. Body habitus 2. Gait abnormalities 3. Limb mal-alignment 4. Joint effusion 5. Skin (eg scars) 6. Reduced range of motion 7. Ligamentous laxity.

2.7 Diagnosis

1.Imaging

Although the diagnosis of knee OA in the most cases can be made by the clinical findings and physical examination, identification of joint damages is necessary for both diagnostic confirmation as well as extent of joint involvement. Conventional plain radiographs of the knee are the first diagnostic procedure as usually requested to demonstrate the structure-pain relationship in knee OA. There is a growing body of work using MRI to examine the correlation between structural findings and symptoms (Watts & Karadsheh, 2018).

Radiography – Recommended views are anteroposterior, lateral and merchant / sunrise views of the knee joint when weight bearing. Findings include: Osteophytes,

Joint space narrowing, Subchondral sclerosis, Subchondral cysts, varus and valgus deformities and bone destruction depending on the stage of osteoarthritis.

MRI findings in knee osteoarthritis include: Cartilage abnormalities, Osteophytes, Bone oedema, Subarticular cysts, Bone attrition, Meniscal tears, Ligament abnormalities Synovial thickening, Joint effusion, Intra-articular loose bodies and Periarticular cysts. Due to its ability to produce high spatial and/or high contrast resolution images, MRI is becoming a favoured too for early detection and surveillance of osteoarthritis of the knee progression.

2.Laboratory findings - Laboratory findings in knee osteoarthritis are non-specific and include normal to increased Erythrocyte Sedimentation Rate and C-reactive protein.

3.Histological findings – Rarely used in clinical practise but also important. Findings include: Loss of superficial chondrocytes, replication and breakdown of the tidemark, fissuring, cartilage destruction with eburnation of subchondral bone

2.8 Differential diagnosis of osteoarthritis of the knee

Several conditions mimic primary osteoarthritis of the knee. Hence important to be sure of the condition. These conditions include: septic arthritis, gout and pseudo gout, polymyalgia rheumatica, tendinitis, bursitis and periarticular fractures.

2.9 Treatment

Treatment options for primary knee OA are pharmacological and non-pharmacological.

2.91. Pharmacological treatment

Pain relief is important in the treatment of primary OA of the knee but not all patients require drug therapy, and those who do may not need it all the time (Cooper et al., 2013).

1. Non-steroidal anti-inflammatory drugs:

They act by inhibition of prostaglandin biosynthesis, which is the first step in all inflammatory disorders. The first step enzyme in the prostaglandin synthetic pathway is prostaglandin G/H synthase, also known as cyclooxygenase or Cox. This enzyme converts arachidonic acid (AA) to unstable intermediated PGG2 and PGH2 and leads to the production of thromboxane A2 (TXA2) and a variety of prostaglandins. There are two forms of cyclooxygenase enzymes, Cyclooxygenase-I (Cox-I) and cyclooxygenase II (Cox-II). Cox-I is a primary constitutive isoform found in most normal cells and tissues while cytokines and inflammatory mediators that accompany inflammation induce Cox-II production. However, Cox-II is constitutively expressed in certain areas of kidney and brain and is induced in endothelial cells by laminar shear forces. Therapeutic doses of NSAIDS reduce prostaglandin biosynthesis by inhibiting the actions of cyclooxygenase enzyme (McAlindon et al., 2014).

There exists a high-quality data that supports the use of NSAIDs in OA. On efficacy, the results are consistent, with good quality patient-oriented evidence (McAlindon et al 2014).

a. **Non-specific cyclooxygenase inhibitors** - The non-specific Cox-inhibitors (e.g. Ibuprofen, Diclofenac, Meloxicam, Aspirin, etc.) inhibit both Cox-I and Cox-II with little selectivity, to slow down prostaglandin synthesis.
b. **Selective Cox-II inhibitors** - The selective Cox-II inhibitors (e.g. Celecoxib, Rofecoxib, and Valdecoxib) have a high predilection for Cox-2, and they gained approval based on superior side effect profile in gut endoscopy studies when compared with other NSAIDS. They have been

found to relieve pain due to osteoarthritis and have less GIT related side effects compared with other NSAIDS (Vaishya et al., 2016).

2. Opiates

Opiates are the drugs derived from opium, and they include the natural products of morphine, codeine, and many semi-synthetic derivatives. The analgesic effect of opioids arises from their ability to directly inhibit the ascending transmission of nociceptive information from the spinal cord dorsal horn and to activate pain control circuits that descend from the midbrain via the rostral ventromedial medullary tract to the spinal cord dorsal horn. Opiates can be classified into short acting, long acting and partial agonist. Both short and long acting opiates and partial agonists have been found to be effective in pain relief and have level 3 evidence in their support. However, the pain relief is limited and in long-term use, these drugs are associated with frequent and sometimes severe side effects. Repeated daily administration of opioid analgesics eventually will produce tolerance and some degree of physical dependence.

3. Paracetamol

It is effective in pain relief among patients with inflammatory osteoarthritis but less efficient than NSAIDS in the treatment of inflammatory arthritis. It is well tolerated (Buckwalter, 2001).

4. Corticosteroids

Intra-articular steroid injections are recommended in situations where the patient has not responded to the simpler analgesics. These are reserved for stages 2 to 3 OA. Their duration of action is limited, usually one month. Oral steroids are not recommended for the treatment of OA because of their modest benefit and high rate of adverse effects (Chapman, 2001).

5. Capsaicin

A 2011 comparative efficacy review concluded that topical capsaicin was superior to placebo for 50% pain reduction but associated with local adverse events (Mc Alindon et al., 2014).

6. Duloxetine

Studies comparing duloxetine with oral placebo found duloxetine efficacious and tolerable for chronic pain associated with OA. Pooled analysis found that 16.3% of the patients who received duloxetine withdrew due to adverse events compared with 5.6% of those receiving placebo. The most commonly reported adverse events included nausea, dry mouth, somnolence, fatigue, constipation, decreased appetite, and hyperhidrosis (Mc Alindon et al., 2014).

2.92. Non-pharmacological treatments:

1. Rehabilitation, education and wellness activity - First line treatment for all patients with symptomatic arthritis. Involves continuous education programs and combination of supervised exercises and home exercises.
2. Weight loss programs - Indicated for patients with symptomatic arthritis and BMI > 25. In the local set up, it is common to get patients in the BMI bracket 25 – 30. BMI over 30 is of great concern. Weight loss programs involve diet and low-impact aerobic exercise.
3. Braces and orthosis for patients with knee joint instability.

Non-pharmacological methods are supported by various researches by Vaishya et al. (2016), Watts and Karadsheh (2018) and Lis (2008).

2.93. Surgery

Surgery is reserved for advanced cases (KL Grade 4) and usually includes knee replacement either total or uni-compartmental (Vaidya et al., 2015).

2.94. Other modalities

Are controversial and have no universal acceptance (Watts & Karadsheh, 2018):

- Acupuncture - AAOS guidelines: strong evidence against
- Viscoelastic joint injections – This procedure is gaining traction but more research needs to be done. (Marcia & Gustavo 2012).
- Glucosamine and chondroitin - AAOS guidelines: strong evidence against
- Needle lavage - AAOS guidelines: moderate evidence against
- Lateral wedge insoles – AAOS guidelines: strong evidence against

As per a Cochrane Review by Townheed et al. (2005) studies testing only the Rotta brand of glucosamine (including low quality and older studies) showed that glucosamine improved pain more than placebo pills. People who took placebo pills had a pain score of 6 points on a 0 to 20 scale. People who took the Rotta brand of glucosamine rated their pain 3 points lower than people who did not take glucosamine. In contrast, Hughes and Carr (2002) did a randomized, double-blind placebo-controlled trial of glucosamine sulphate efficacy but did not find any difference between placebo and glucosamine/chondroitin sulphate in the management of pain in primary osteoarthritis of the knee. In addition, more than 40 clinical studies of the effects of chondroitin and glucosamine sulphate in patients with osteoarthritis have been conducted, unfortunately many of these studies have important limitations. Despite their limitations, the majority of the studies, including some double blind investigations, show that oral glucosamine and chondroitin sulphate provide some symptomatic relief

in selected patients and side effects are minimal (Enas & Abeer., 2014 ; Buckwalter et al., 2001).

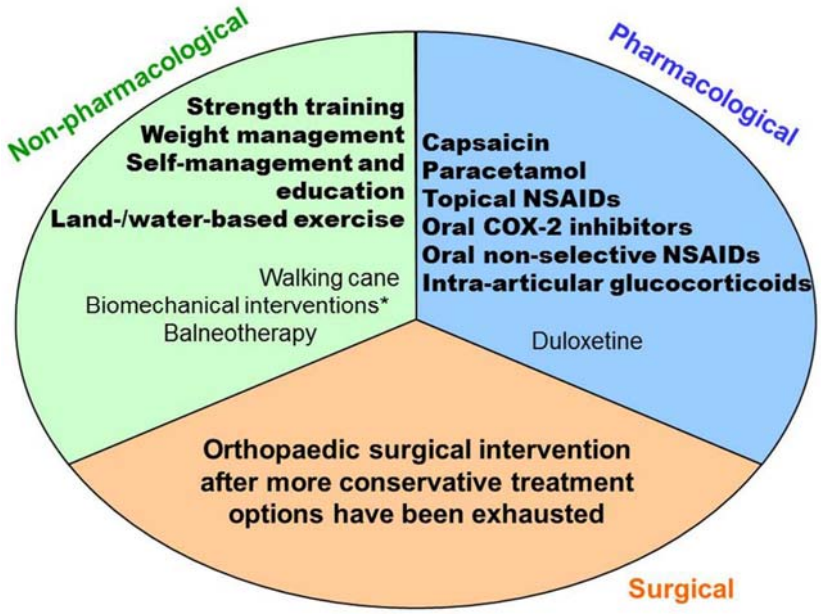


Figure 9: Management of knee osteoarthritis

Table 6: Non-operative management of Osteoarthritis of the knee (Osteoarthritis Research Society Guidelines, OARSI, 2014)

Core Treatments	**Knee only OA without co-morbidities**	**Knee only OA with co-morbidities**	**Multiple joint OA without co-morbidities**	**Multiple joint OA with co-morbidities**
-Exercises -Weight management -Strength training -Health education	-Biomechanical interventions -Intra-articular steroids -Topical NSAIDs -Oral Cox 2 Inhibitors -Capsaicin -Oral Non selective NSAIDs -Duloxetine and -Paracetamol	-Biomechanical interventions -Walking cane -Topical NSAIDS -Intra-articular steroids	-Oral Cox 2 Inhibitors -Intra-articular steroids -Oral non-selective NSAIDS -Biomechanical interventions -Duloxetine -Paracetamol	-Balneotherapy -Biomechanical interventions -Intra-articular steroids -Oral Cox 2 inhibitors -Duloxetine

2.10. Treatment outcomes of osteoarthritis of the knee

Numerous studies have been done to determine outcome of various non-operative treatment methods for osteoarthritis of the knee. Systemic reviews and previous guidelines are consistently under review to come up with appropriate guidelines.

The Osteoarthritis Research Society International (OARSI) guidelines of 2014 are the most consistent outcome guidelines based on extensive research on osteoarthritis of the knee. Thirteen experts from relevant medical disciplines (primary care, rheumatology, orthopaedics, physical therapy, physical medicine and rehabilitation, and evidence-based medicine), three continents and ten countries (USA, UK, France, Netherlands, Belgium, Sweden, Denmark, Australia, Japan, and Canada) and a patient representative comprised the Osteoarthritis Guidelines Development Group (OAGDG). Based on previous OA guidelines and a systematic review of the OA literature, 29 treatment modalities were considered for recommendation. Evidence published subsequent to the 2010 OARSI guidelines was based on a systematic review conducted by the OA Research Society International (OARSI) evidence team at Tufts Medical Centre, Boston, USA. Medline, EMBASE, Google Scholar, Web of Science, and the Cochrane Central Register of Controlled Trials were initially searched in first quarter 2012 and last searched in March 2013. Included evidence was assessed for quality using Assessment of Multiple Systematic Reviews (AMSTAR) criteria, and published criticism of included evidence was also considered. To provide recommendations for individuals with a range of health profiles and OA burden, treatment recommendations were stratified into four clinical sub-phenotypes. Consensus recommendations were produced using the RAND/UCLA Appropriateness Method and Delphi voting process. Treatments were recommended as Appropriate, Uncertain, or Not Appropriate, for each of four clinical sub-phenotypes and accompanied by 1-10 risk and benefit scores.

Table 7: Treatment outcomes of osteoarthritis of the knee (OARSI, 2014)

No	Treatment	Recommendation	Level of evidence	Quality of evidence
1	Acupuncture	Uncertain	SR and meta-analysis of RCTs	Good
2	Spa therapy (Balneotherapy)	Appropriate	SR and meta- analysis of RCTs	Fair
3	Biomechanical interventions	Appropriate	SR of RCTSs and non-randomized clinical trials	Fair
4	Walking cane	Appropriate	Single blind RCT	Fair
5	Crutches	Uncertain	Expert consensus	Poor – No trials
6	Exercise	Appropriate	SR and meta-analysis of RCTs	Good
7	Health education	Appropriate	SR and meta- analysis of RCTs	Good
8	Weight management	Appropriate	SR and meta- analysis of RCTs	Good
9	T.E.N.S	Uncertain	SR of RCTs	Good
10	Paracetamol	Appropriate	SR and meta- analysis of RCTs	Good
11	Capsaicin	Appropriate	SR of RCTs	Good
12	Steroids (Intra-articular)	Appropriate	SR and meta- analysis of RCTs	Good
13	Chondroitin	Uncertain	SR and meta- analysis of RCTs	Good
14	Glucosamine	Uncertain	SR and meta- analysis of RCTs	Good
15	Diacerein	Uncertain	SR and meta- analysis of RCTs	Good
16	Duloxetine	Appropriate	SR and meta- analysis of RCTs	Fair
17	Hyaluronic acid	Uncertain	SR and meta- analysis of RCTs	Good
18	NSAIDS	Appropriate	SR and meta- analysis of RCTs	Good
19	Oral opioids	Uncertain	SR and meta- analysis of RCTs	Good
20	Risedronate	Uncertain	SR and meta- analysis of RCTs	Good

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

The study was a hospital based descriptive prospective study where new patients with a diagnosis of primary osteoarthritis of the knee were followed up in the MTRH orthopaedic clinic for a duration of 6 months and the outcome of their treatment determined.

Being a descriptive prospective study with a limited population, no randomisation or blinding was done for the participants.

3.2 Study area

This study was carried out at the Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya. MTRH is a national level 6 Referral Hospital located in Uasin-Gishu County, in the North Rift region of Western Kenya. This is about 310 kilometres Northwest of Nairobi, the capital city of Kenya.

As a level 6 hospital, it offers various services including: internal medicine, general surgery, obstetrics and gynaecology services, oncology services, renal Medicine, paediatric medicine, paediatric surgery, kidney transplants, alcohol and rehabilitation services, mental health, spinal and neurosurgical operations, specialized orthopaedics and trauma, cardiology and free maternity services among others.

Moi Teaching and Referral Hospital was started in 1917 with a bed capacity of 60 to cater for the Africans Health Needs. It later served as a District Hospital before attaining referral status vide Legal Notice No. 98 of 12 June 1998 of the State Corporations Act

(Cap 446). Currently, it is the second largest referral hospital in Kenya with a bed capacity of 991 patients. Average in-patients at any one time are 1200 and about 1500 outpatients per day. It serves the greater western Kenya region representing about 40% of the country's population. It also serves eastern Uganda and parts of Southern Sudan. The total catchment population is approximately 24 million (MTRH, 2019)

MTRH is also the teaching hospital for Moi University College of Health Sciences that trains both undergraduate medical students and post graduate students distributed across several programs.

The study was conducted at the specialised orthopaedic clinic in the hospital.

3.3 Study population

This included new patients being managed for primary osteoarthritis of the knee at the MTRH between 1st January 2017 and 30th June 2018 who met the eligibility criteria.

The patients being seen were patients new to MTRH, even if they had been seen in other primary and secondary facilities, and not newly diagnosed knee OA patients.

3.4 Subject selection

3.4.1 Eligibility criteria

All new patients managed for primary osteoarthritis of the knee within the period of study and from whom an informed consent was obtained.

3.4.2 Exclusion criteria

- All patients with diagnosed gout
- Patients with secondary osteoarthritis of the knee
- Patients with rheumatoid arthritis. (Ruled out with ACR criteria)
- Patients currently continuing treatment for OA of the knee at MTRH
- Patients who had undergone total knee replacement.

- Patients with multiple joint osteoarthritis eg hip and knee

3.5 Sampling method

Patient selection was by Census method where every eligible participant was enrolled into the study. A total of 72 participants were enrolled but 4 patients were lost to follow up during the course of the study.

3.6 Data collection instruments and technique

Data was collected using structured interviewer-administered questionnaires. Patients with knee O.A. were followed up in the orthopaedic clinic for a duration of 6 months.

Information recorded included patients 'responses together with medical information recorded in the patient's file i.e.: patient's demographic data, prior co-morbidities, duration between onset of symptoms and presentation to hospital, general state of patient, dominant signs and symptoms, diagnosis and definitive management. Further information was acquired through physical examination of the patients.

The Western Ontario Mc Master Osteoarthritis Index(WOMAC) questionnaire was used to collect data on the patient's symptoms and scored appropriately to provide an objective assessment of the patient's physical condition and track their response to treatment at 0, 3 and 6 months of treatment.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a widely used, proprietary set of standardized questionnaires used by health professionals to evaluate the condition of patients with osteoarthritis of the knee and hip, including pain, stiffness, and physical functioning of the joints. The WOMAC has also been used to assess back pain, rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus

erythematosus, and fibromyalgia. It can be self-administered and was developed at Western Ontario and McMaster Universities in 1982 (Bellamy, 2004).

The WOMAC measures five items for pain (score range 0–20), two for stiffness (score range 0–8), and 17 for functional limitation (score range 0–68). Physical functioning questions cover everyday activities such as stair use, standing up from a sitting or lying position, standing, bending, walking, getting in and out of a car, shopping, putting on or taking off socks, lying in bed, getting in or out of a bath, sitting, and heavy and light household duties. The total scores for the various parameters are totalled to a maximum of 96. Higher scores indicate severe condition as opposed to lower total scores (Woolacott et al., 2010).

The main method of administration is oral. It can also be administered by telephone and email with valid results (Bellamy et al., 2011; Theiler et al., 2002).

The test-retest reliability of the WOMAC varies for the different subscales. The pain subscale has not been consistent across studies, but it generally meets the minimum standard. The physical function subscale is more consistent and has a stronger test-retest reliability. The stiffness subscale has also been shown to have consistent test-retest reliability.

The WOMAC Index has been used extensively in clinical trials, and has generally been shown to exhibit greater or comparable responsiveness to change than other tests.

The Questionnaires were administered at 0, 3 and 6 months. The first questionnaire denoted 0 months was administered at the beginning of the study. This was followed

up with questionnaires at 3 and 6 months to check the response of the patient to treatment.

The questionnaire was mainly administered orally. However, for patients who did not come for follow up visit, mobile phone conversation and filling of the questionnaire was done. Oral administration of the WOMAC questionnaire at the beginning of the study was for 72 patients. At 3 months, oral administration was for 52 patients; 16 patients were interviewed through mobile phone conversation. At 6 months, oral administration of the WOMAC questionnaire was for 49 patients; 19 patients were interviewed through mobile phone conversation.

X-rays of the affected joint were taken at the commencement of the study and the state of the joint recorded. This was used to classify the grade of osteoarthritis of the knee using the Kellgren-Lawrence grading. Information on treatment for the patients was gotten from the patient's files/ records.

Compliance to medications was determined by asking the patients about missed doses. Adverse effects were recorded in the Ministry of Health, suspected adverse drug reaction reporting form.

All filled questionnaires were checked for completeness and coded accordingly. The data was entered in MS Excel at the end of each day for storage and backup.

3.7 Data analysis

Data was encrypted for security and confidentiality.

A back up of the same data using memory drive to cushion against loss of data was made. Data analysis was done using SPSS version 23. Results were summarised using descriptive statistics mean, median, interquartile range and standard deviation.

Chi square and Fischer's exact test were used to test for association of osteoarthritis of the knee with BMI and hypertension respectively.

Results were presented in the form of figures, tables and graphs.

3.8 Ethical consideration

Ethics review and approval to conduct the study was sought from the MTRH/Moi University IREC committee before the study commenced. Approval was given with formal approval number FAN: IREC 1284.

Permission from Moi Teaching and Referral Hospital was granted before the study commenced. Approval letter: Ref: ELD/MTRH/R.6/VOL.II/2008.

Written informed consent was obtained from every participant before participating in the study. The consent forms were in both English and Kiswahili depending on the language the patients understood best.

All patients' information was kept confidential protected by password only known to the researcher and there were no incentives given to the participants.

The study was a voluntary participation and no patient was denied treatment whether he or she consented or not.

Patients were not coerced and had a right to withdraw from the study.

Once the thesis is ready, an oral presentation will be conducted and also be published in peer review journals.

3.9 Study limitations

High cost of drugs for treatment of primary osteoarthritis of the knee which hindered compliance. This was especially for chondroitin and glucosamine sulphate. Also due to the long duration of use which led to an increase in total cost of medication for most patients. This was mitigated through adherence counselling of patients on proper drug use.

Collection of data was done for a period of 6 months for every patient which was limited. This is due to primary osteoarthritis of the knee being a chronic condition that requires long term follow up.

This being a prospective study, loss to follow up was anticipated. This was mitigated by recording patients and relatives contacts and reminding patients of their scheduled clinic visits. For those who could not attend the clinic, mobile phone conversation was used to follow up the patients with valid results.

CHAPTER FOUR

4.0 RESULTS

4.1 Introduction

The findings were based on 72 patients who were managed for primary knee O.A. at the MTRH between 1st January 2017and 30th June 2018. The main outcome variable of the study was the treatment outcome of osteoarthritis which was measured by WOMAC index categorized into mild arthritis symptoms (0-32), moderate arthritis symptoms (33-64) and severe arthritis symptoms (65-96).

Patients were followed up for six months at which point the main outcome was measured. Of the 72 patients enrolled 4 were lost to follow-up hence outcome variable (WOMAC) was not measured on the four.

Oral administration of the WOMAC questionnaire at the beginning of the study was for 72 patients. At 3 months, oral administration was for 52 patients whereas 16 patients were interviewed through mobile phone conversation. At 6 months, oral administration of the WOMAC questionnaire was for 49 patients whereas 19 patients were interviewed through mobile phone conversation.

4.2 Social demographics characteristics

Table 8: Social demographic characteristics of participants

Variable	Categories	Frequency/median(IQR)	Percentage / range
Age	Median(IQR)	64 (56, 69)	26 - 88
Weight	Median(IQR)	73.5 (63.5, 87.5)	45 - 110
Sex	Male	14	19.44 %
	Female	58	80.56 %
BMI	Underweight	5	6.94 %
	Normal weight	30	41.67 %
	Overweight	18	25.00 %
	Obese	19	26.39 %
Occupation	Farmer	49	68.06 %
	Business	11	15.28 %
	Others	12	16.67 %

Majority (80.6%) of respondents were females. Main occupation was farming (68.1%). Age range was between 26 - 88 years with median age of 64(56, 69).

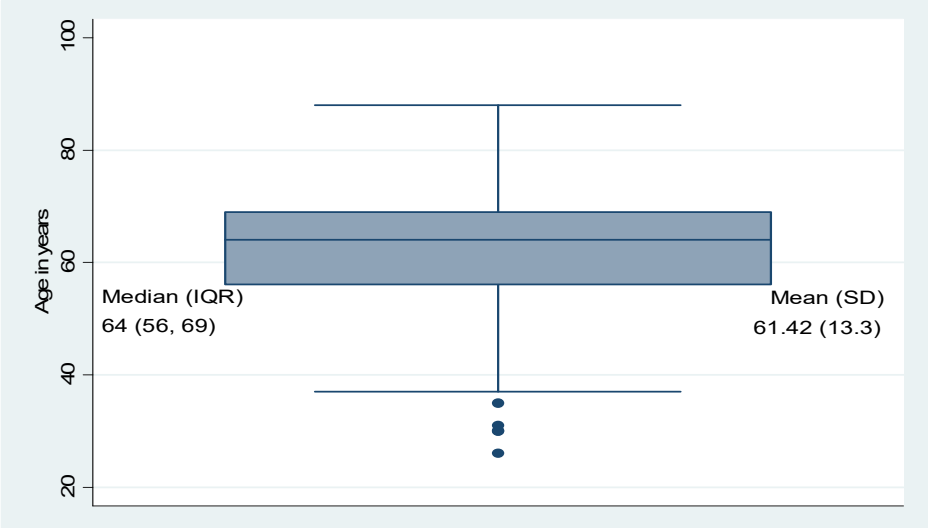


Figure 10: Box plot showing age distribution of participants

About 75% of the respondents were aged above 55 years with median age of 64 (56, 69) years and ranged from 26 to 88 years.

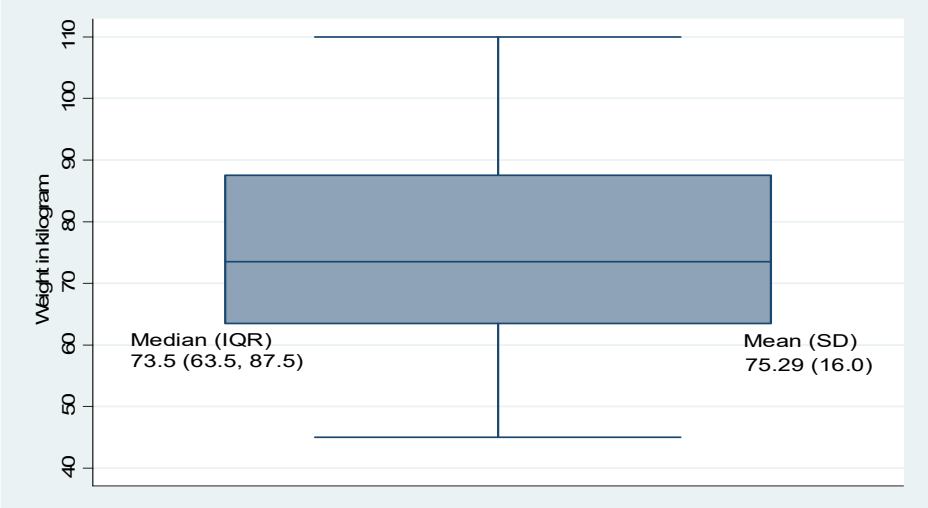


Figure 11: Box plot showing weight distribution of participants

The weight of respondents ranged from 45 to 110 kilograms with median of 73.5 (63.5, 87.5) where 75% of the respondents were weighing above 62 kilograms.

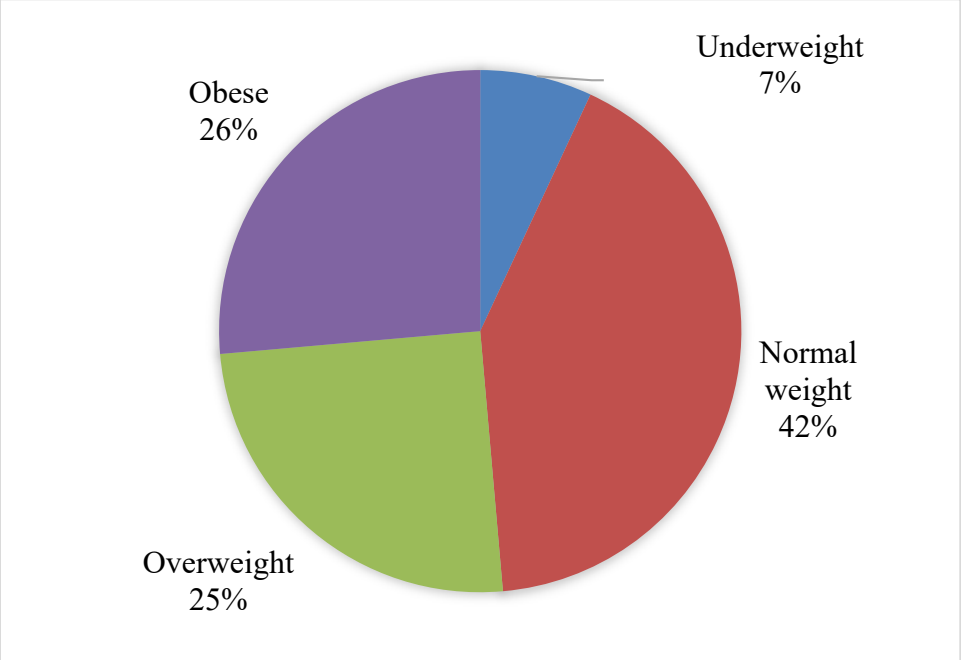


Figure 12: Pie chart showing BMI of participants

Most participants were of normal weight (42%) followed by obese and overweight participants at 26% and 25% respectively. Only 7% were underweight.

4.3 Medical history

Table 9: Medical history of participants

Variable	Categories	Frequency	Percentage
Painful knee	Right	33	45.83
	Left	24	33.33
	Both	15	20.83
Duration of symptoms	< 1 year	21	29.17
	1 – 5 years	38	52.78
	6 – 10 years	8	11.11
	> 10 years	5	6.94
Medical condition	Yes	20	27.78
	No	52	72.22
Type of condition	Hypertension	9	45.00
	BPH	2	10.00
	Gynaecological conditions	2	10.00
	BPH, HTN, DM	1	5.00
	CSDH	1	5.00
	Diabetes Mellitus	1	5.00
	Associated fracture	1	5.00
	SLE	1	5.00
	Spondylitis	1	5.00
	Vulvular heart disease	1	5.00

The most affected knee was right being mentioned by 45.8% of the respondents while 20.8% said both legs were painful. Majority (81.95%) had had the pain for less than 6 years and only 20(27.8%) had comorbidities.

4.4 Radiological findings

Table 10: Radiological findings of participants at the beginning of the study

Findings	Frequency	Percentage
Normal	3	4.17
Osteophytes	68	94.44
Joint space narrowing (<50%)	69	95.83
Subchondral cysts	18	25.00
Subchondral sclerosis	31	43.06
Severe joint space narrowing (>50%)	27	37.50
Bone ends deformity	21	29.17

The table above shows the findings on x-ray, out of 72 patients only 3(4.2%) had normal x-ray, majority (95.8%, 94.4%) had joint space narrowing and osteophytes respectively.

Table 11: Kellgren Lawrence grading of patients at the beginning of the study

Grade	Frequency	Percentage %
0	3	4.16
1	7	9.72
2	23	31.95
3	18	25.00
4	21	29.17
Total	72	100

Most patients were between Kellgren Lawrence grade 2 to grade 4 severity of knee OA. Three patients had normal radiological findings.

4.5 Treatment

Table 12: Non-operative treatment methods for patients with knee OA

Method		Frequency	Percentage %
Selective Cox 2 inhibitors NSAIDS + Chondroitin / glucosamine sulphate		25	36.76
Selective Cox 2 inhibitors NSAIDs		13	19.12
Non-selective Cox inhibitors NSAIDs		9	13.24
Both NSAIDS groups		8	11.76
Non-selective Cox inhibitors NSAIDS+ Chondroitin / glucosamine sulphate		7	10.29
Both NSAIDS + Chondroitin / glucosamine sulphate		2	2.94
Opioids		2	2.94
Steroids		2	2.94
Other non-pharmacological methods (combined with medication)	Lifestyle modification	68	100.00
	Physiotherapy	50	73.53
	Knee brace	15	22.06

All the patients were on lifestyle modification (100%). The main non-operative treatment method used was selective Cox 2 inhibitors NSAIDS combined with chondroitin/glucosamine sulphate at 36.76% followed by selective Cox 2 inhibitors NSAIDS at 19.12%. Very few patients were on steroids and opioids at 2.94% each.

The main non-pharmacological methods used were physiotherapy (73.53%) and knee bracing (22.06%) which were used in combination with pharmacological interventions.

4.6 Outcome

Table 13: Outcome using WOMAC index

Treatment	Categories	Frequency	Percentage
Initial disease severity symptoms	Mild	14	19.44
	Moderate	54	75.00
	Severe	4	5.56
Disease severity symptoms at 3 months	Mild	58	85.29
	Moderate	9	13.24
	Severe	1	1.47
Final disease severity symptoms	Mild	46	67.65
	Moderate	21	30.88
	Severe	1	1.47

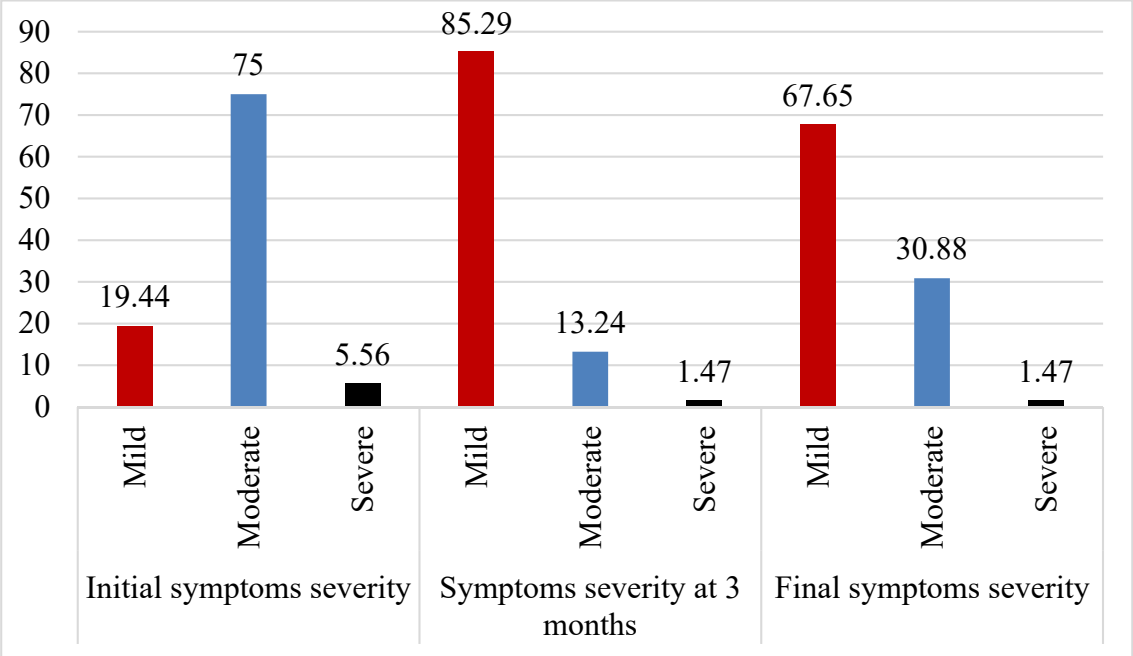


Figure 13: Bar graph of outcome using WOMAC index.

There was improved symptomatology outcome over 6 months. A percentage of 19.44% of patients had mild symptoms which increased to 85.29% of patients at 3 months and 67.65% of patients at 6 months of treatment.

Patients with moderate symptoms dropped from 75% at the beginning of the study to 13.24% at 3 months and 30.88% at 6 months.

Patients with severe symptoms dropped from 5.56% at beginning of the study to 1.47% at 3 months and 6 months.

No patient was pain free at the end of the study.

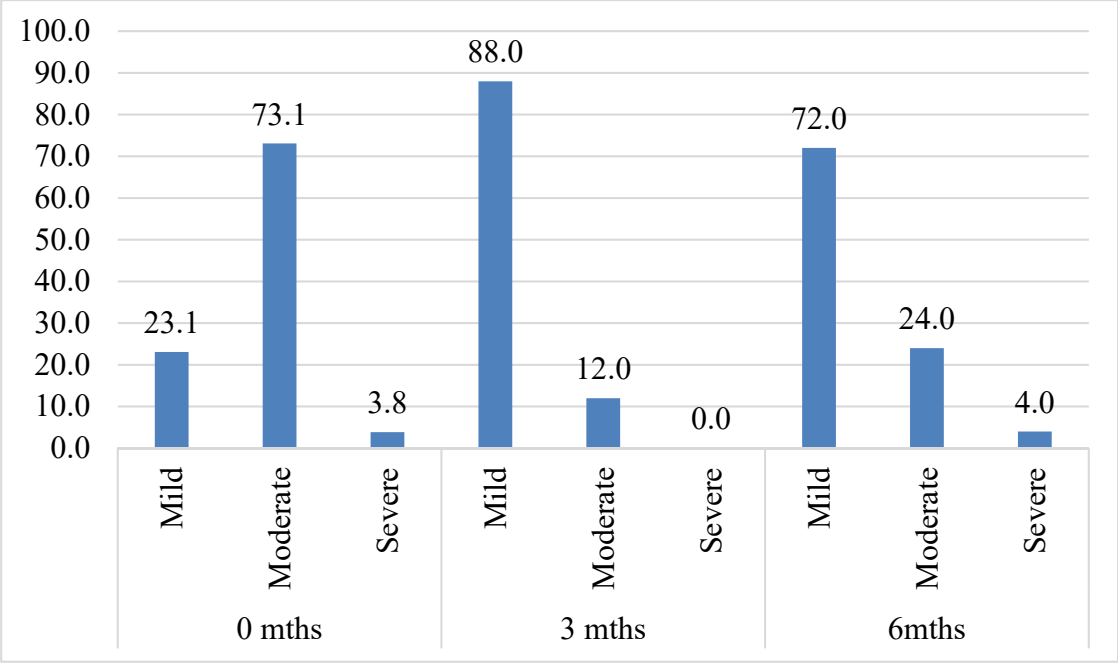


Figure 14: Bar graph of outcome of combined treatment with Selective Cox 2 inhibitor NSAIDS + Chondroitin / Glucosamine sulphate.

Patients on management with a combination of selective Cox 2 NSAIDS and chondroitin/glucosamine sulphate improved in symptomatology at 3 months with a decrease in improvement at 6 months. Mild symptoms were observed in 23.1% of patients at the beginning of study which improved to 88% of the population at 3 months and 72% of the population at 6 months.

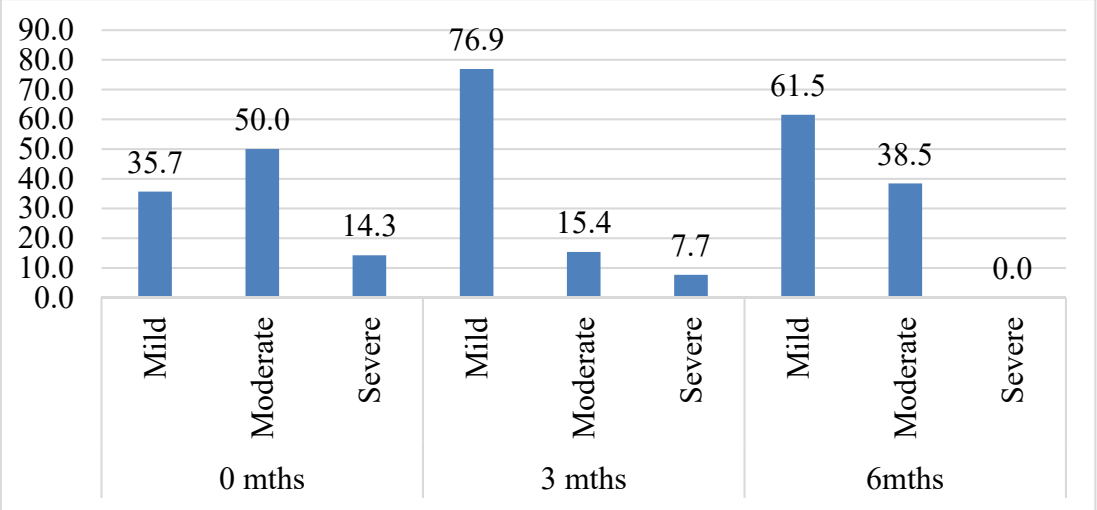


Figure 15: Bar graph of outcome of outcome of treatment with Selective Cox 2 inhibitor NSAIDS.

Patients on management with selective Cox 2 inhibitor NSAIDS showed improvement at 3 and 6 months of treatment. Mild symptoms were seen in 35.7% of patients at the beginning of the study and in 76.9% of patients at 3 months and 61.5% of patients at 6 months. Severe symptoms were seen in 14.3% of patients at the onset of the study which dropped to 7.7% and 0.00% at 3 and 6 months respectively.

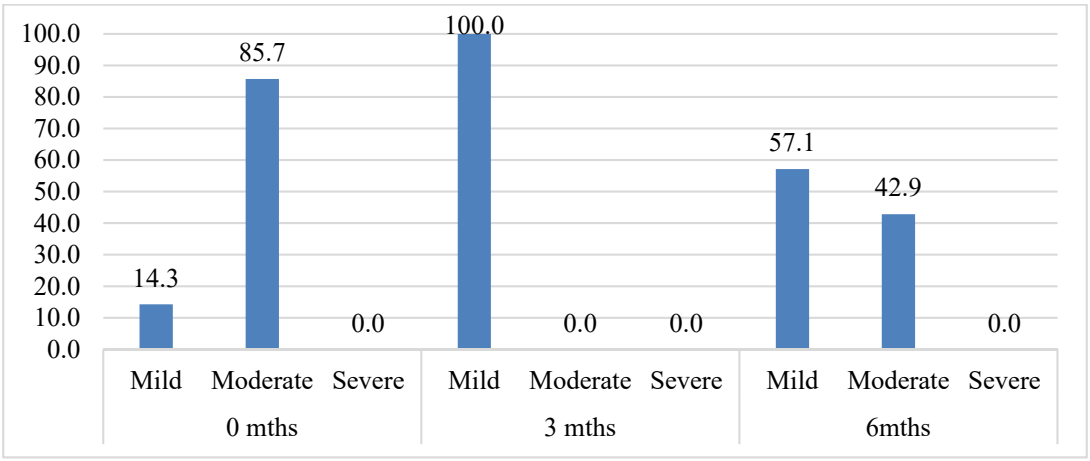


Figure 16: Bar graph of outcome of combined treatment with Non-selective Cox inhibitor NSAIDS + Glucosamine / Chondroitin sulphate.

Improvement in symptomatology was noted for patients after 3 and 6 months of treatment with Non-selective Cox inhibitor NSAIDS and glucosamine/chondroitin sulphate combination.

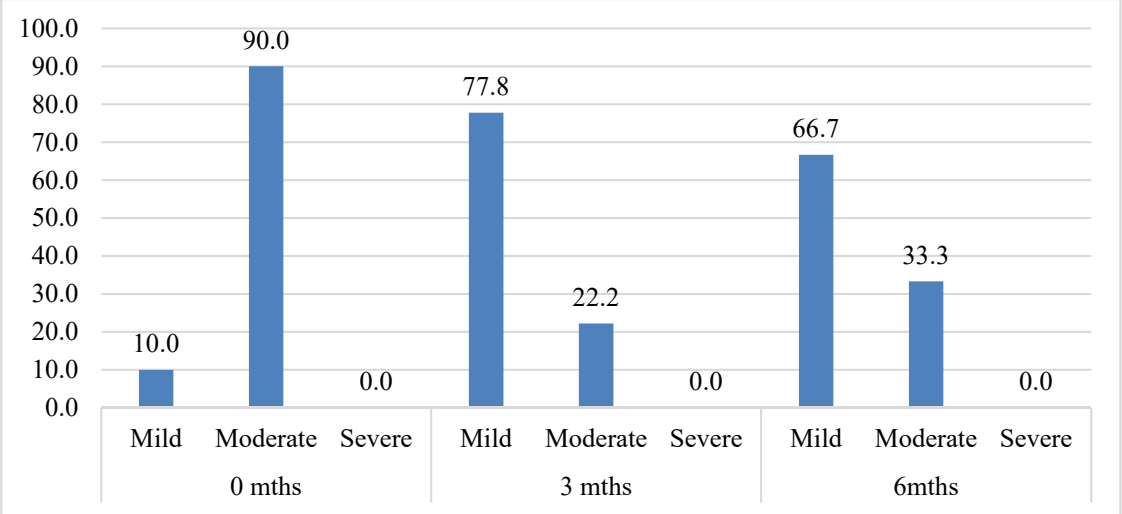


Figure 17: Bar graph of outcome of treatment with Non-selective Cox inhibitor NSAIDS.

Majority of the patients had moderately severe symptoms at the beginning of the study (90% of patients). These improved to mild symptoms in 77.8% of patients and 66.7% of patients at 3 and 6 months respectively after treatment with non-selective Cox inhibitor NSAIDS.

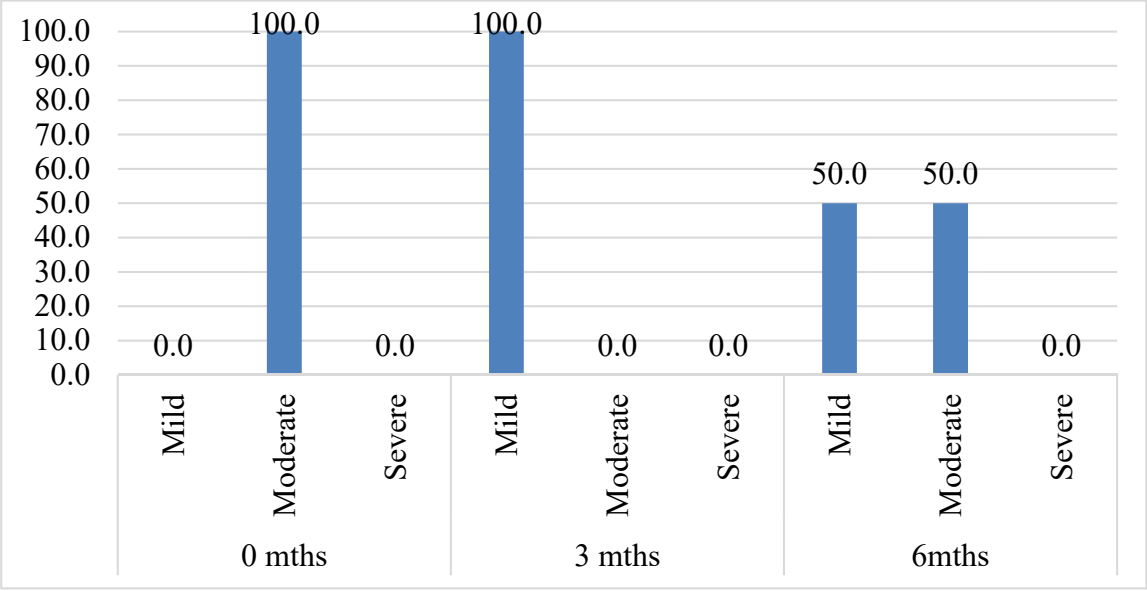


Figure 18: Bar graph of outcome of treatment with both NSAID group drugs plus Glucosamine/chondroitin sulphate.

Patients with moderate symptoms showed marked improvement at 3 months with 100% of patients reporting mild symptoms from moderate symptoms at the beginning of the study after treatment with both NSAID group drugs and chondroitin/glucosamine sulphate. This dropped at 6 months with 50% of patients reporting mild symptoms and 50% reporting moderate symptoms.

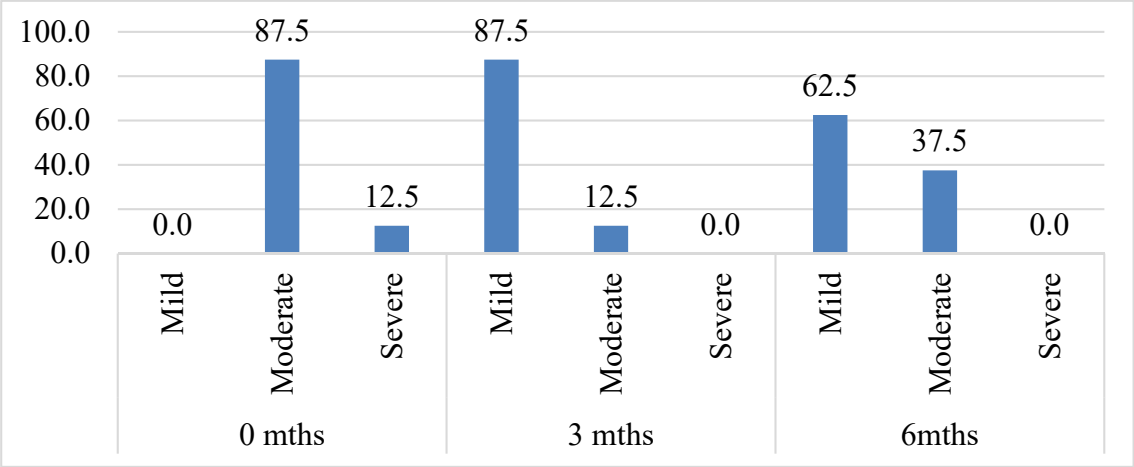


Figure 19: Bar graph of outcome of treatment with both NSAID groups.

Patients with moderate symptoms improved to mild symptoms at 3 and 6 months of treatment. A percentage of 87.5% of patients reported moderate symptoms at the beginning of the study. These improved to mild symptoms after treatment in 87.5% and 62.5% of patients at 3 and 6 months respectively.

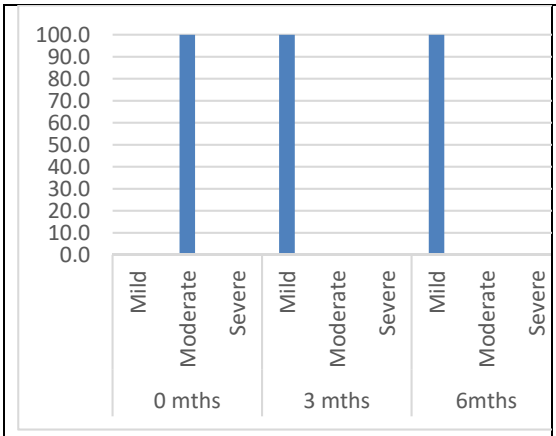


Figure 20 : Bar graph of outcome of treatment with opioids

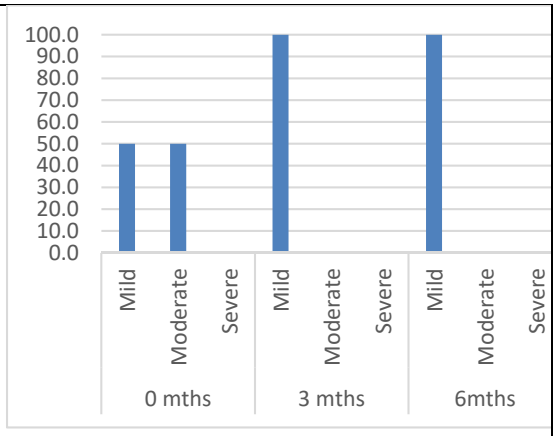


Figure 21: Bar graph of outcome of treatment with steroids.

Patients on opioids and steroids showed improvement after 3 and 6 months of treatment.

4.7 Association

Table 14: Association between outcome of treatment of knee OA and BMI and hypertension

		WOMAC		
Variable	**Category**	**Mild**	**Moderate**	**P-value**
BMI	Underweight/normal	21	10	0.881[c]
	Overweight/obese	25	11	
Hypertension	No	4	4	0.335[f]
	Yes	7	2	

[c] Chi Square, [f] Fisher's Exact test

In the study, there was no association established between outcome of treatment of Osteoarthritis of the knee and Body Mass Index and hypertension. (p-value = 0.881 by Chi Square test, and p value = 0.335 by Fisher's Exact test), respectively.

CHAPTER FIVE

5.0 DISCUSSION

Studies determining treatment outcomes of non-operative methods used in treatment of primary osteoarthritis of the knee are limited in MTRH.

5.1 Sociodemographic indicators:

Primary Knee osteoarthritis tends to affect the elderly persons mainly due to degenerative joint disease. The median age of the study was an age of 64 years (IQR 56 -69) with a mean duration of 6 years. This is in agreement with a local study by Nour et al. (2013) who determined the median age of OA to be 61.4 years with a mean duration of 5years.

The study also established that majority of participants were women at 80.56%. This concurs with a study by Nour et al. (2013) who found 85% of patients with primary osteoarthritis of the knee were female. An international Irish study by French et al. (2015) published in the European Journal of Public health, Vol 26,2015 established a prevalence of 76% in females and 24% in male persons. The main cause of this is oestrogen decrease post-menopausal which leads to bone weakness/fragility.

The main occupation of the patients was farming at 49%. Farming in the area of study, that is, Uasin Gishu County and the surrounding regions is highly manual and is rarely automated. This leads to increased strain on the joints predisposing to osteoarthritis of the knee. This is in agreement with studies by Watts and Karadsheh (2019) who determined that physical strain aggravates osteoarthritis of the knee.

5.2 Co-morbidities in patients with primary osteoarthritis of the knee

Obesity is a chronic metabolic disease which poses serious risks for the development of any serious illness including hypertension, diabetes mellitus, heart disease and musculoskeletal disease. The evidence linking obesity to primary OA has been accumulating. The risk of developing OA in overweight and obese patients has been the topic of several studies. This study found the occurrence of primary osteoarthritis of the knee in overweight patients to be 25% and 26% in obese patients respectively. This was in contrast with local studies which found a much higher co-morbidity of osteoarthritis with overweight and obese patients at 32% and 41% respectively (Nour et al., 2013).

Association studies done determined no association between primary osteoarthritis of the knee and obesity in this study. This was due to a limited hospital population which did not entirely reflect the whole population.

A total of 20 out of 72 patients with primary osteoarthritis of the knee had co-morbidities. The most frequently occurring co-morbidity was hypertension in 27.78% of patients with co-morbidities. This agreed with studies by Behzad (2011) who found hypertension as the most frequently occurring co-morbidity in patients with primary osteoarthritis of the knee. Association studies found no relation between primary osteoarthritis of the knee and hypertension. This was probably due to limited population size.

All the patients were non-smokers. This was mainly because most of them were women, and there is a lot of cultural negativity associated with women smoking in the area of study, that is, Uasin Gishu County and the surrounding areas. This contrasted with a study by Dube (2016) who established a prevalence of 6.2% of patients with primary

osteoarthritis as smokers. Studies by Chin and Mehta (2008) and studies by Buckwalter et al. (2001) also found positive association between smoking and primary osteoarthritis of the knee. This was not the case in this study.

5.3 Non-operative treatment types:

The main non-operative treatment types used were Non-steroidal anti-inflammatory drugs (NSAIDs) either singly or in combination with glucosamine/chondroitin sulphate. A percentage of 55.88% of patients were on selective Cox 2 inhibitor NSAIDS whereas 23.53% were on non-selective Cox inhibitor NSAIDS with good outcome. A percentage of 14.7% were also on both groups of NSAIDS with good outcome. This was in agreement with studies by Vaishya et al. (2016) who found that there exists high-quality data that supports the use of NSAIDs in OA. On efficacy, the results are consistent, with good quality patient-oriented evidence. However, there may be side effects related to gastrointestinal, renal, and cardiovascular systems to consider that may offset their place in OA therapy. The literature supports the use of Paracetamol in OA (level A), but NSAIDs are more effective than Paracetamol in pain relief.

The role of steroids in treatment of knee OA at MTRH was limited with only 2.94% of patients treated with either oral or intra-articular steroids. This was mainly due to availability and cost of inta-articular steroids as well as the side effect profile. This was in agreement with systemic reviews and meta-analysis of randomized clinical trials by McAlindon et al. (2014) which recommends short term intra-articular steroids for symptomatic relief. Long term use is not recommended due to side effect profile which includes: osteoporosis, cushion states, muscle mass loss, thromboembolism, spontaneous fractures and myopathies.

Patients treated with opioids were 2.94% of total patients with the main drug being tramadol. The limited use was due to the side effect profile of tolerance for opioids and the fact that they were not readily available. This is in agreement with studies by Vaishya et al. (2016) which advises that the pain relief of opioids is limited and in long-term use, these drugs are associated with tolerance and some degree of physical dependence. When pain is due to a chronic condition like OA, measures other than opioid drugs should be employed to relieve pain if they are efficient and available.

A moderately high proportion of study patients were on glucosamine and chondroitin sulphate. Up to 49.99% of patients were on this treatment. This was in combination with analgesic medication. As per a Cochrane Review by Townheed et al. (2005) studies testing only the Rotta brand of glucosamine (including low quality and older studies) showed that glucosamine improved pain more than placebo pills. People who took placebo pills had a pain score of 6 points on a 0 to 20 scale. People who took the Rotta brand of glucosamine rated their pain 3 points lower than people who did not take glucosamine. In contrast, Hughes and Carr (2002) did a randomized, double-blind placebo-controlled trial of glucosamine sulphate efficacy but did not find any difference between placebo and glucosamine/chondroitin sulphate in the management of pain in primary osteoarthritis of the knee. In addition, more than 40 clinical studies of the effects of chondroitin and glucosamine sulphate in patients with osteoarthritis have been conducted, unfortunately many of these studies have important limitations. Despite their limitations, the majority of the studies, including some double blind investigations, show that oral glucosamine and chondroitin sulphate provide some symptomatic relief in selected patients and side effects are minimal (Buckwalter et al., 2001).

For this study, the exact efficacy of glucosamine and chondroitin could not be established singly as the drugs were given in combination with analgesia medication.

Non-medical managements including: lifestyle modification, functional bracing, physiotherapy and exercises were also used to improve patient symptoms.

Viscosupplementation, which is injection of intra-articular hyaluronic acid, into the joint to improve lubrication and mobility was not found to be in use at MTRH. This was due to cost and ease of availability. However, it has been found to be gaining prominence worldwide with benefits ranging from 6 months to two years, but more research needs to be done (Marcia & Gustavo, 2012).

All patients were put on more than one method of treatment to try and manage the disease aggressively.

5.4 Outcome of treatment

The WOMAC index was used to gauge the patient's symptomatology and response to treatment during the beginning, at 3 months and after 6 months of treatment. It is a widely used, proprietary set of standardized questionnaires used by health professionals to evaluate the condition of patients with osteoarthritis of the knee and hip, including pain, stiffness, and physical functioning of the joints.

The 3 months' duration of study is the standard period of treatment of osteoarthritis where one expects response. Hence the use of 3 and 6 months as reasonable outcome periods for the study. This agrees with the USA FDA recommendation of 12 weeks being the standard time for treatment of chronic conditions.

Most patients improved over the 6 months of the study. Only 19.4% of patients had mild symptoms (WOMAC score 0-32 points) at the beginning of the study which

increased to 85.3% at 3 months, then dropped to 67.6% at 6 months. Moderate symptoms (WOMAC score 33-95 points) were observed in 75.0% of respondents at the beginning of the study, which dropped to 13.1% at 3 months and 30.1% of respondents at the end of the study. Severe symptoms (WOMAC score greater than 65 points) were observed in 5.6% of respondents at the beginning of the study and 1.5% of respondents at 3 and 6 months. These patients with severe symptoms were advised to undergo knee replacement surgery. The study is in agreement with international evidence-based guidelines for the management of patients with hip and knee osteoarthritis (OA) which recommend to start with a combination of non-operative treatments, and using surgical intervention only if a patient does not respond sufficiently to non-surgical treatment options (Vaishya et al., 2016). The study also agrees with an Egyptian randomized clinical trial by Enas and Abeer (2014) which showed that 12-week oral administration of alpha – D glucosamine and NSAIDS could significantly improve primary knee OA pain, stiffness and limitation in function.

No patient was completely pain free at the end of the study. This is because there is no known cure for OA, treatment designed for the individual patient were for pain reduction, improved joint mobility and limitation of functional impairment. This is in agreement with previous studies by Nour et al. (2013) and McLindon et al. (2014).

The following non-operative treatment methods were used:

- Combination of Selective Cox inhibitor NSAIDS and Chondroitin/Glucosamine sulphate
- Selective Cox inhibitor NSAIDS as monotherapy
- Combination of Non-selective Cox inhibitor NSAIDS and Chondroitin/Glucosamine sulphate

- Non-selective Cox inhibitor NSAIDS as monotherapy
- Both groups of NSAIDS
- Intra-articular steroids
- Opioid analgesics mainly tramadol
- Lifestyle modification
- Knee bracing
- Physiotherapy

The above treatment methods led to improvement in symptoms at 3 and 6 months of treatment. However, this improvement was more marked at 3 months as compared to 6 months. This is in contrast to a study by Cooper et al. (2013) which established consistent improvement of symptoms in one year with monthly use of systemic NSAIDS with improvement in symptoms being better as time progressed. The main reason for decreased improvement in symptoms after 3 months in the study was attributed to compliance issues to medication. This was due to the high cost of drugs which were out of reach of some of the patients and adverse effect profile of medications mainly epigastric pain. Some patients also developed emotional exhaustion due to long term medication use without full remission of symptoms. This was mitigated through adherence counselling of the patients.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

1. Primary osteoarthritis of the knee had high occurrence in female, elderly patients at MTRH.
2. Hypertension was the most common co-morbidity seen in patients with primary osteoarthritis of the knee at MTRH.
3. NSAIDs were the main non-operative treatment type for primary osteoarthritis of the knee at MTRH, either singly or in combination with glucosamine/chondroitin sulphate. Non pharmacological management types including: lifestyle modification, bracing and physiotherapy were also used to improve patient outcome at MTRH.
4. Improvement in symptomatology was noted for patients at 3 and 6 months of non-operative management.

6.2 Recommendations

1. Lifestyle modification – Patient education, Exercise and weight reduction to assist in management of primary OA of the knee.
2. Comprehensive review of all patients with primary OA of the knee at the clinic to diagnose, treat and follow up of other co-morbidities.
3. Standard protocols for management of primary knee OA containing NSAIDS should be developed to aid in reduction of morbidity.
4. A prospective study with a longer follow up period for patients with primary OA of the knee.

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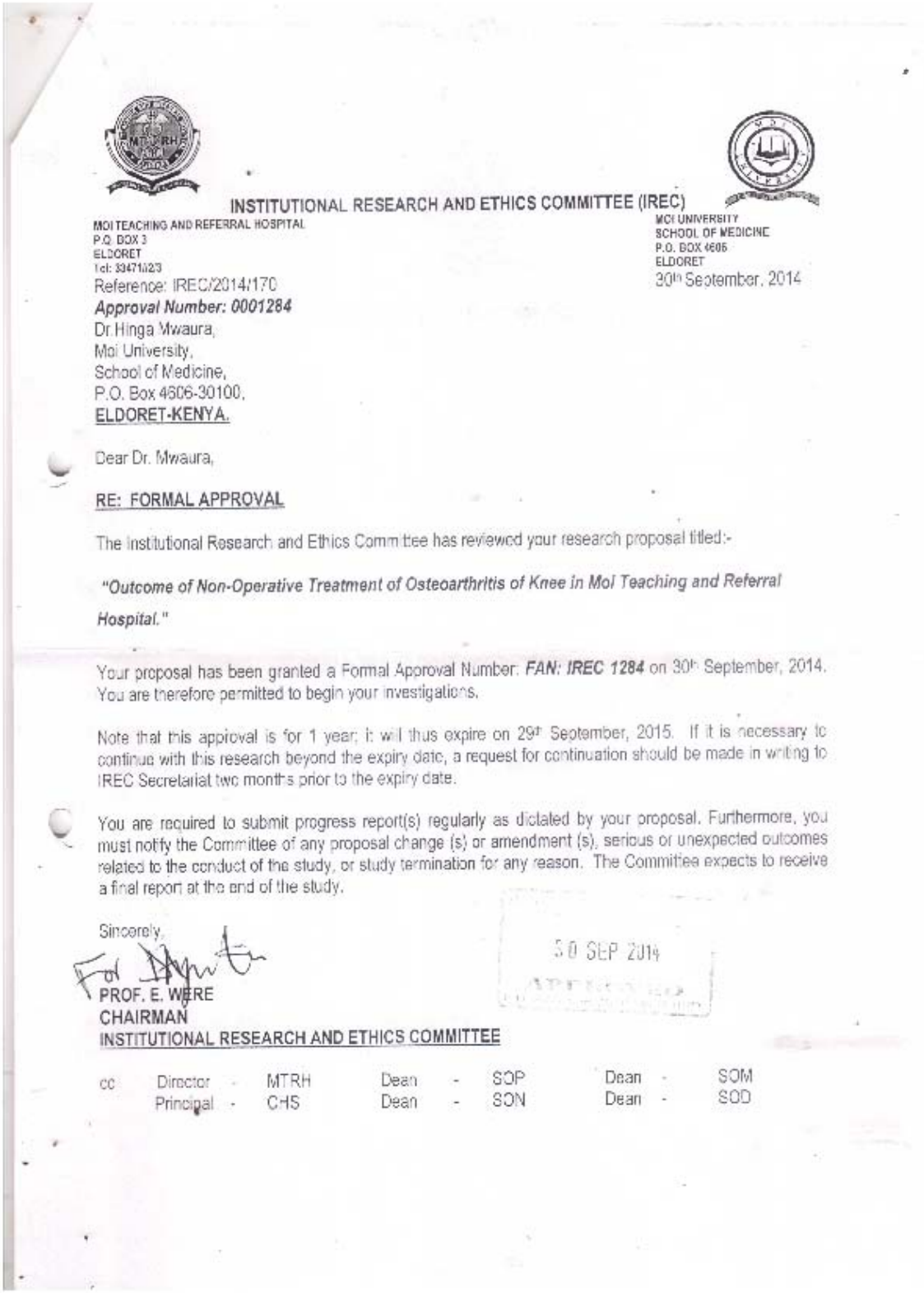
APPENDICES

Appendix 1: IREC Approval



INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2014/170
30th September, 2014

Approval Number: 0001284

Dr Hinga Mwaura,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Mwaura,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Outcome of Non-Operative Treatment of Osteoarthritis of Knee in Moi Teaching and Referral Hospital."

Your proposal has been granted a Formal Aporoval Number: ***FAN: IREC 1284*** on 30th September, 2014. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 29th September, 2015. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

30 SEP 2014

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc Director - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix 2: IREC Extension Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2014/170
Approval Number: 0001284

26th January, 2018

Dr. Hinga Mwaura,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
26 JAN 2018
APPROVED
P. O. Box 4606 - 30100 ELDORET

Dear Dr. Mwaura,

RE: CONTINUING APPROVAL

The Institutional Research and Ethics Committee has reviewed your request for continuing approval to your study titled:-

"Outcome of Non-Operative Treatment of Osteoarthritis of Knee in Moi Teaching and Referral Hospital".

Your proposal has been granted a Continuing Approval with effect from 26th January, 2018. You are therefore permitted to continue with your study.

Note that this approval is for 1 year; it will thus expire on 25th January, 2019. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH
Principal - CHS
Dean - SOM
Dean - SPH
Dean - SOD

Scanned by CamScanner

Appendix 3: MTRH Approval

IREC/2014/170 F-COPY

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke

P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008

30th September, 2014

Dr.Hinga Mwaura,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:

"Outcome of Non-Operative Treatment of Osteoarthritis of Knee In Moi Teaching and Referral Hospital."

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR.JOHN KIBOSIA

DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD,HRISM

Appendix 4: Introductory Letter

Dr Humphrey Hinga Mwaura,

P O Box 13204 – 20100,

Nakuru, Kenya.

Tel 0722745296.

Date: 6th January 2017.

Dear Sir/Madam,

Ref: Introduction

I hereby want to inform you that I am currently conducting a study on outcome of non-operative treatment of patients with primary osteoarthritis of the knee at Moi Teaching and Referral Hospital, Eldoret, Kenya.

Once the study has been completed, the results will be used to provide more information on outcome of non-operative treatment of primary osteoarthritis of the knee. This may help in provision of better management of patients in the future.

Yours Faithfully,

Humphrey Hinga Mwaura.

Appendix 5: Consent Form

My name is Dr Humphrey Hinga Mwaura and I am a postgraduate student at Moi University School of Medicine.

I am conducting a study on the outcome of treatment of patients with primary osteoarthritis of the knee at Moi Teaching and Referral Hospital (MTRH), Eldoret, Kenya.

The information obtained will assist the hospital and doctors in general to decide on the best method of treatment of primary osteoarthritis of the knee. Results of this research will be compared with studies done elsewhere.

I request your permission to be involved in this study. The study involves you getting the best treatment offered in this hospital for your condition thereafter you will be followed up at the orthopaedic clinic to find out the outcome of the treatment. You will be asked certain questions to determine your progress.

Whatever information we gathered will be kept confidential and will not be shared with anyone except members of our study team. Your identity will not be revealed to others. Your participation in this study is entirely voluntary and you can stop me anytime for any clarification you might need or if uncomfortable to continue. However, I hope you will participate in this study to the end.

At this time, do you want to ask me anything about this study?

Consent:

I, ……. having been informed about this study to my satisfaction and all my questions and concerns having been addressed, do give consent to participate in the study.

Signed: ……Date ……

Signature of interviewer: ……Date…….

Fomu idhini

Jina langu ni Daktari Humphrey Hinga Mwaura na mimi ni mwanafunzi katika chuo kikuu cha Moi. Nahitimu katika idara ya upasuaji.

Ninafanya utafiti juu ya matokeo ya matibabu ya wagonjwa wenye ugonjwa wa baridi yabisi kwa magoti katika hospitali ya rufaa ya Moi, mjini Eldoret, Kenya.

Habari inayopatikana itasaidia hospitali na madaktari kwa ujumla kuamua juu ya njia bora ya matibabu ya ugonjwa wa baridi yabisi kwa magoti. Matokeo ya utafiti huu yatalinganishwa na masomo yaliyofanywa mahali pengine.

Naomba ruhusa yako kuhusika katika utafiti huu. Utafiti unajumuisha kupata matibabu bora inayotolewa katika hospitali hii kwa hali yako baadaye utafuatwa katika kliniki ya mifupa ili kujua matokeo ya matibabu. Utaulizwa maswali kadhaa ili kuamua maendeleo yako.

Habari yoyote ambayo tumekusanya itahifadhiwa kwa siri na haitashirikiwa na mtu yeyote isipokuwa washiriki wa timu yetu ya masomo. Utambulisho wako hautafunuliwa kwa wengine. Ushiriki wako katika utafiti huu ni wa hiari kabisa na unaweza kunisimamisha kwa wakati wowote kwa ufafanuzi wowote ambao unaweza kuhitaji au ikiwa haifai kuendelea. Walakini, natumai kuwa utashiriki katika utafiti huu hadi mwisho.

Kwa wakati huu, unataka kuniuliza chochote juu ya utafiti huu?

Dhibitisho:

Mimi, ……. baada ya kupewa habari juu ya utafiti huu kwa kuridhika kwangu na maswali yangu yote na maswala yangu yote yameshashughulikiwa, napeana ruhusa ya kushiriki katika utafiti.

Sahihi ya Mshiriki.....Tarehe.....

Sahihi ya Mkuu wa Uchunguzi.....Tarehe.....

Appendix 6: Data collection questionnaire

1. Name of patient ……..... IP No……
2. Age ……..…. Sex…….……Weight ……..…...…….……
3. Occupation……Residence……..…
4. Mobile number…….
5. Which of your knees is painful: Right knee:  Left knee: 
6. For how long have you had the knee pain:

   Right knee:  <1year  <5years  <10years 

   >10yrs

   Left knee:  <1year  <5years  <10years 

   >10yrs

7. Have you ever been injured before to the knee:  Yes  No

   If yes, what kind of injury and when……

8. Do you smoke:  Yes  No.

   If yes, how many cigarettes per day and how many years……

9. Do you suffer from any other medical condition:……..……

10. What kind of treatment is the patient on for Osteoarthritis: **(Clinician to specify):**

a. Lifestyle modification: (specify)……...……

b. NSAIDs: (list drugs) ……

c. Steroids: (list drugs) …….

d. Opioids: (list drugs) ……

e. Surgery: (specify type) …….……..

f. Cartilage regenerators: (list drugs)……

g. Others (specify type)…….....

11. What are the radiological findings on the patient: **(Clinician to tick x-ray findings)**

State of knee joint:	**Tick**
Normal knee joint x-ray	
Presence of osteophytes in knee joint	
Joint space narrowing	
Presence of subchondral cysts	
Presence of subchondral sclerosis	
Severe joint space narrowing	
Deformity of bone ends	

Appendix 7: WOMAC Index Questionnaire

Your Full Name: _____ **Today's Date:** _____/_____/_____

Month Day Year

WOMAC OSTEOARTHRITIS INDEX

1. The following questions concern the amount of pain you are currently experiencing in your knees. For each situation, please enter the amount of pain you have experienced in the past 48 hours.

		None	mild	moderate	severe	extreme
A. Walking on a flat surface	A.	☐	☐	☐	☐	☐
B. Going up or down stairs	B.	☐	☐	☐	☐	☐
C. At night while in bed	C.	☐	☐	☐	☐	☐
D. Sitting or lying	D.	☐	☐	☐	☐	☐
E. Standing upright	E.	☐	☐	☐	☐	☐

2. Please describe the level of pain you have experienced in the past 48 hours for each one of your knees.

		None	mild	moderate	severe	extreme
A. Right knee	A.	☐	☐	☐	☐	☐
B. Left knee	B.	☐	☐	☐	☐	☐

3. How severe is your stiffness after first awakening in the morning?

None	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

4. How severe is your stiffness after sitting, lying, or resting later in the day?

None	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

5. The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities, please indicate the degree of difficulty you have experienced in the last 48 hours, in your knees.

What degree of difficulty do you have with:

		None	mild	moderate	severe	extreme
A. Descending (going down) stairs	A.	☐	☐	☐	☐	☐
B. Ascending (going up) stairs	B.	☐	☐	☐	☐	☐
C. Rising from sitting	C.	☐	☐	☐	☐	☐
D. Standing	D.	☐	☐	☐	☐	☐
E. Bending to floor	E.	☐	☐	☐	☐	☐
F. Walking on a flat surface	F.	☐	☐	☐	☐	☐
G. Getting in/out of car	G.	☐	☐	☐	☐	☐
H. Going shopping	H.	☐	☐	☐	☐	☐
I. Putting on socks/stockings	I.	☐	☐	☐	☐	☐
J. Rising from bed	J.	☐	☐	☐	☐	☐
K. Taking off socks/stockings	K.	☐	☐	☐	☐	☐
L. Lying in bed	L.	☐	☐	☐	☐	☐
M. Getting in/out of bath	M.	☐	☐	☐	☐	☐
N. Sitting	N.	☐	☐	☐	☐	☐
O. Getting on/off toile	O.	☐	☐	☐	☐	☐
P. Heavy domestic duties (mowing the lawn, lifting heavy grocery bags)	P.	☐	☐	☐	☐	☐
Q. Light domestic duties (such as tidying a room, dusting, cooking)	Q.	☐	☐	☐	☐	☐

Appendix 8: American College of Rheumatology diagnostic criteria

Diagnostic Criteria (1987 Revised Criteria for Diagnosis of Rheumatoid arthritis)
1. Morning stiffness ≥ 1hour
2. Swelling in ≥ 3 joints
3. Rheumatoid nodules
4. Radiographic changes of the hand including bony erosions and decalcification
5. Symmetric arthritis
6. Serum rheumatoid factor
7. Arthritis of the hand (Metacarpophalangeal, Proximal interphalangeal joints) and wrist
Interpretation: Must have ≥4 of 7 criteria for a 6-week period

Appendix 9: Suspected adverse drug reaction reporting form

(rev.2.0)

IN CONFIDENCE

MINISTRY OF HEALTH
PHARMACY AND POISONS BOARD
P.O. Box 27663-00506 NAIROBI
Tel: (020)-3562107 Ext 114, 0720 608811, 0733 884411 Fax: (020) 2713431/2713409
Email: pv@pharmacyboardkenya.org

☐ Initial Report
☐ Follow-up Report

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

REPORT TITLE: .....

NAME OF INSTITUTION: ..... INSTITUTION CODE: .....

ADDRESS: ..... CONTACT: .....

COUNTY: .....

****

PATIENT NAME / INITIALS: ..... IP/OP. NO.: ..... D.O.B / AGE: .....

PATIENT ADDRESS: ..... WARD /CLINIC: ..... GENDER: ☐ Male ☐ Female
(NAME / NUMBER)

ANY KNOWN ALLERGY:
☐ No
☐ Yes (specify).....

PREGNANCY STATUS
☐ Not Applicable
☐ Not Pregnant
☐ 1st Trimester ☐ 2nd Trimester ☐ 3rd Trimester

WEIGHT: ..... Kg
HEIGHT: ..... cm

DIAGNOSIS: (what was the patient treated for) .....

DATE OF ONSET OF REACTION: .....

BRIEF DESCRIPTION OF REACTION: .....

.....

LIST OF *ALL* DRUGS USED IN THE LAST 3 MONTHS PRIOR TO REACTION. IF PREGNANT, INDICATE DRUGS USED DURING THE 1ST TRIMESTER (include OTC and herbals) {use rear side of this form for additional drugs}	BRAND NAME	DOSE	ROUTE AND FREQUENCY	DATE STARTED	DATE STOPPED	INDICATION	TICK (√) SUSPECTED DRUG(S)
1.							
2.							
3.							
4.							
5.							

SEVERITY OF THE REACTION
(Refer to scale overleaf)
☐ Mild
☐ Moderate
☐ Severe
☐ Fatal
☐ Unknown

ACTION TAKEN:
☐ Drug withdrawn
☐ Dose increased
☐ Dose reduced
☐ Dose not changed
☐ Unknown

OUTCOME:
☐ Recovering / resolving
☐ Recovered / resolved
☐ Requires or prolongs hospitalization
☐ Causes a congenital anomaly
☐ Requires intervention to prevent permanent damage
☐ Unknown

CAUSALITY OF REACTION
(Refer to scale overleaf)
☐ Certain
☐ Probable / Likely
☐ Possible
☐ Unlikely
☐ Conditional / Unclassified
☐ Unassessable / Unclassifiable

ANY OTHER COMMENTS: .....

.....

NAME OF PERSON REPORTING: ..... DATE: .....

E-MAIL ADDRESS: ..... PHONE NUMBER: .....

DESIGNATION: ..... SIGNATURE: .....

You need not be certain… just be suspicious!

Your support towards the National Pharmacovigilance system is appreciated
Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the event.
Patient's identity is held in strict confidence and programme staff is not expected to and will not disclose reporter's identity in response to any public request.
Information supplied by you will contribute to the improvement of drug safety and therapy in Kenya. Once completed please send to:
The Pharmacy and Poisons Board on the above address

Suspected adverse drug reaction reporting form (continued)

EXPLANATORY NOTES

CONFIDENTIALITY
All information collected in this form, identities of the reporter and patient, will remain confidential.

WHAT TO REPORT
An Adverse Drug Reaction (ADR) is defined as a reaction that is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis or treatment of a disease, or for modification of physiological function.

Report all suspected adverse experiences with medications, especially those where the patient outcome is:

- Death
- Life-threatening (real risk of dying)
- Hospitalization (initial or prolonged)
- Disability (significant, persistent or permanent)
- Congenital anomaly
- Required intervention to prevent permanent impairment or damage

Report even if:

- You are not certain if the drug caused the reaction
- You do not have all the details

WHO CAN REPORT
All healthcare professionals (clinicians, dentists, nurses, pharmacists, physiotherapists, community health workers etc) are encouraged to report. Patients (or their next of kin) may also report

WHAT HAPPENS TO THE SUBMITTED INFORMATION
All information submitted is handled in strict confidence. The Pharmacy and Poisons Board will assess causality and statistical analysis on each form. Data will periodically be used for reviews and suggest any interventions that may be required to the Ministry of Health. Data will also be submitted periodically to the Uppsala Monitoring Center- the WHO Collaborating Centre for International Drug Monitoring in Sweden.

SUBMISSION OF FOLLOW-UP REPORTS
It is important to tick the appropriate box on the top right corner of the front page to indicate whether the report is an initial (original) report or is a follow-up (subsequent) report.
It is very important that follow-up reports are identified and linked to the original report.

WHERE TO REPORT
After completing this form, please forward the same to your Pharmacy Department for onward submission, or mail directly, to:

PHARMACY AND POISONS BOARD
Lenana Road
P.O. Box 27663-00506 NAIROBI
Tel: (020)-3562107 Ext 114, 0720 608811, 0733 884411
Fax: (020) 2713431/2713409
Email: pv@pharmacyboardkenya.org

Please use the space provided below for any further information. You may attach more pages to this form if required.

.....
.....
.....

LIST OF ALL DRUGS USED IN THE LAST 3 MONTHS PRIOR TO REACTION (include OTC and herbals)	BRAND NAME	DOSE	ROUTE AND FREQUENCY	DATE STARTED	DATE STOPPED	INDICATION	TICK (√) SUSPECTED DRUG(S)
6.							
7.							
8.							
9.							
10.							

Criteria for Assessment of Severity of an ADR

Mild	• The ADR requires no change in treatment with the suspected drug • The ADR requires that the suspected drug be withheld, discontinued or otherwise changed. No antidote or other treatment is required • No increase in length of stay.
Moderate	• The ADR requires that the suspected drug be withheld, discontinued or otherwise changed, and/or an antidote or other treatment is required. • Increases length of stay by at least one day • The ADR is the reason for admission
Severe	• The ADR requires intensive medicare care • The ADR causes permanent harm to the patient
Fatal	• The ADR either directly or indirectly leads to the death of the patient
Unkown	• When you have no information about the ADR

WHO-UMC Causality Assessment Scale

Causality Term	Assessment
Certain	• Event of laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically *(i e. an objective and specific medical disorder or a recognized pharmacological phenomenon)* • Rechallenge satisfactory, if necessary
Probable / Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal lacking or unclear
Unlikely	• Event or laboratory test abnormality with a time to drug that makes a relationship improbable (but not impossible) • Diseases or other drugs provide plausible explanations
Conditional/ Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed or • additional data under examination
Unassessable/ unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because of insufficient or contradictory information • Data cannot be supplemented or verified

Your support towards the National Pharmacovigilance system is appreciated
Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the event.
Patient's identity is held in strict confidence and programme staff is not expected to and will not disclose reporter's identity in response to any public request.
Information supplied by you will contribute to the improvement of drug safety and therapy in Kenya. Once completed please send to:
[illegible] and Poisons Board on the above address

Appendix 10: Budget

NO	ACTIVITY	UNIT COST (ksh)	NUMBER	TOTAL COST(Ksh)
1	Stationery -Printing and photocopy -Binding of proposal -Biro pens	-	-	10,000 / =
2	Proposal writing and binding	10,000 /=	5	50,000 /=
3	Transport -To collect data -To follow up patients	100 /=	100 participants	10,000 /=
4	Communication expenses -Internet expenses -Telephone expenses	-	-	15,000 /=
5	Consultant charges	10,000 /=	1	30,000 /=
6	Contingencies	-	-	5,000 /=
7	Laptop purchase	70,000/=	1	70,000/=
8	**TOTAL**			**190,000 /=**

Appendix 11: Work Plan.

NO	ACTIVITY	DATE	DEADLINE	BY WHO	WHERE
1	PROPOSAL DRAFTING	APRIL 2014	JULY 2014	DR MWAURA	MUSOM
2	PROPOSAL REVIEW WITH SUPERVISOR	JULY 2014	JULY 2014	DR LELEI DR AYUMBA	MUSOM
3	PROPOSAL SUBMISSION TO IREC	JULY 2014	JULY 2014	DR MWAURA	MUSOM
4	DATA COLLECTION	JAN 2017	JUNE 2018	DR MWAURA	MTRH ORTHOPAEDIC CLINIC
5	DATA ANALYSIS	JULY 2017	SEP 2018	DR MWAURA	MUSOM
6	DATA PRESENTATION	OCT 2018	NOV 2018	DR MWAURA	MUSOM
7	WRITING OF THESIS	NOV 2018	APRIL 2019	DR MWAURA	MUSOM
8	DEPARTMENTAL DEFENSE	APRIL 2019	APRIL 2019	DR MWAURA ALL FACULTY	FACULTY BOARDROOM MUSOM
9	MOCK THESIS DEFENCE	MAY 2019	MAY 2019	DR MWAURA ALL FACULTY	FACULTY BOARDROOM MUSOM
10	FINAL DEFENCE OF THESIS	SEP 2020	SEP 2020	DR MWAURA ALL FACULTY	FACULTY BOARDROOM MUSOM
11	PUBLICATION OF THESIS	DEC 2020	DEC 2020	DR MWAURA	EAJOS