EVALUATION OF PAIN MANAGEMENT AMONG PATIENTS WITH RHEUMATOID ARTHRITIS AT KENYATTA NATIONAL HOSPITAL

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A RESEARCH DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF PHARMACY IN CLINICAL PHARMACY IN THE SCHOOL OF PHARMACY OF THE UNIVERSITY OF NAIROBI.

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DEDICATION

To my precious family: my husband Rogers, my children Natasha and Natalie, my mum Linnet, my dad Johnstone and my siblings Mercy, Brian, Cynthia, Cyril and Frankline. Thank you all for your words of encouragement, unwavering support and push for tenacity that kept me going.

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ABBREVIATIONS AND ACRONYMS

ADR	Adverse Drug Reaction
AOR	Adjusted Odds Ratio
BPI	Brief Pain Inventory
COX	Cyclooxygenase
COR	Crude Odds Ratio
DMARDs	Disease Modifying Antirheumatic Drugs
ERC	Ethics Review Committee
KNH	Kenyatta National Hospital
MMAS-8	Morisky Medication Adherence Scale-8
NSAIDs	Non Steroidal Anti Inflammatory Drugs
PI	Principal Investigator
PPI	Proton Pump Inhibitors
RA	Rheumatoid Arthritis
TNF	Tumor Necrotic Factor
UON	The University of Nairobi
WHO	World Health Organization

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OPERATIONAL DEFINITION OF TERMS

Rheumatoid arthritis is a systemic progressive autoimmune disease characterized by chronic inflammation of the joints.

Pain is an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage.

An adverse drug reaction is an unwanted or harmful reaction experienced after the administration of a drug or combination of drugs under normal conditions of use. It may occur following a single dose or prolonged administration of a drug.

Adherence refers to whether a patient takes medication according to the instructions given on the prescription

ABSTRACT

Background: Rheumatoid arthritis is a progressive chronic autoimmune systemic inflammatory disease that causes significant pain, functional disability and joint destruction. Pain is the most distressing symptom of this disease and thus largely affects the activities of living of these patients. Despite medications and aggressive forms of treatment, many patients still experience continuous pain and stiffness. There is need to reduce, control and prevent rheumatic pain through proper management of inflammation.

Objective: To evaluate pain management among patients with rheumatoid arthritis at Kenyatta National Hospital between June and September 2018.

Methodology: A cross sectional study was used. One hundred and fifteen patients with a clinical diagnosis of rheumatoid arthritis who met the inclusion criteria from the rheumatology clinic, were conveniently sampled and recruited to the study. Data on pain control was collected using structured questionnaires. Data analysis was carried out using STATA version 14 software. The descriptive data was presented as proportions and frequencies in tables,pie charts and graphs. The association between pain control and other variables was explored using Fischer's exact test and Logistic regression model. Inferential analysis was carried out at 0.05 level of significance.

Results: One hundred and fifteen participants were enrolled to the study.There was a female predominance (n = 103,89.8%) and a mean age of 48 years old (SD = 16.4). Disease Modifying Anti Rheumatic Drugs were the most prescribed class of drugs (n = 111,96.5%) with methotrexate (n = 74,64.4%) and hydroxychloroquine (n = 50,43.5%) being the most prescribed drugs. Fifty one (44.4%) participants had at least one cormobidity reported. Hypertension being the most prevalent. Abdominal pain and headache were the most reported adverse drug reactions. Low adherence levels were reported in almost three quarters of the participants. The main reasons for non adherence included; lack of finances, severity of the disease,duration of treatment, forgetfulness and drug being unaffordable. Forty eight (51.6%) participants reported experiencing pain on the day of the interview and on average, participants had inadequate pain control. Employment status was a predictor of pain control (COR = 0.085,95% CI = 0.009 - 0.796; *P* value = 0.031). The unemployed participants had 0.085 times the odds of having adequate pain control compared to their employed counterparts.Walking ability predicted the adequacy of pain control. Participants who reported no interference with their ability to walk were 5.540 times more likely to have adequate pain control (COR = 5.540,95% CI = 1.562-19.660; *P*=0.008. Normal work and adequacy of pain control were significantly associated (COR = 4.347,95% CI = 1.315 -14.369; *P* = 0.016). Enjoyment of life was an independent predictor of adequacy of pain control (AOR = 14.075,95% CI = 1.842 - 107.514; *P* = 0.011). Participants who had no interference with their enjoyment of life had 14.075 times the odds of having adequate pain control when all other factors are held constant. The independent predictors of the level of adherence included; regular exercise (AOR = 4.235,95% CI = 1.131-15.849; *P* = 0.032), severity of the disease (AOR = 0.171,95% CI = 0.029 - 1.011; *P* = 0.052), unafforadable drug (AOR = 0.163,95% CI = 0.027 - 0.971; *P* = 0.046) and relations with other people (AOR = 0.232,95% CI = 0.072 - 0.749; *P* = 0.015).

Conclusion: Rheumatoid arthritis was most prevalent in females and DMARDs were the first line of treatment. Occurences of adverse drug reactions and the level of adherence significantly impacted on the adequacy of pain control. Pain was generally inadequately controlled.

Recommendation: Enhance patient education on rheumatoid arthritis and its management and also ensure intensive adherence counselling to the patients.

CHAPTER ONE: INTRODUCTION

1.1 Background to the study

Rheumatoid arthritis (RA) is one of the most commonly diagnosed chronic, autoimmune, systemic inflammatory disease (1). It causes significant pain, functional disability and joint destruction (2).Globally, there is regional variability in the reported cases of RA in adult population and the worldwide prevalence is estimated to be between 0.5% and 1%. For instance, studies carried out in India among the Pima and Chippewa Indians have reported a higher prevalence of 5.3% and 6.8% respectively. China and Japan populations have reported low occurrences (3). Rural South Africa and West Africa revealed that RA was a mild and uncommon disorder with prevalence of less than 0.1%. This is contrary to the Ugandan experience that reported severe cases of disease, high rate of seropositivity and a range of extra articular features. Reports from Kenya, Central Africa and urban South Africa mirrored the Ugandan experience (4). A study done in Kenya by Bagg *et al* showed that seventy six patients with a diagnosis of RA had manifestations that resembled those seen in the Caucasian populations. However,these manifestations differed from those reported in West Africa and rural South Africa (5). A study done by Denhaerynck *et al* showed that women are three times more affected than men and onset is at any age but peaks between 40 and 60 or older for men. The prevalence increases with age (6).

Patients with RA suffer debilitating symptoms due to the progressive inflammatory nature of the disease (7). Multiple joints are affected especially the small joints of the hands, feet, wrists, elbows, shoulders, hips, knees, jaws and ankles. Joint involvement is often symmetrical with a few exceptions. Patients present with pain, stiffness and swelling in the multiple joints. The morning stiffness lasts more than an hour. Systemic symptoms of fatigue, low grade fever, weight loss, and mild anaemia may occur with active disease. Extra articular involvement includes rheumatoid nodules, vasculitis, pulmonary complications and ocular manifestations (1). Patients with rheumatoid arthritis experience significant pain that adversely affects their activities of living. Pain is first caused by inflammation in the joints and later on by damage to the joints. It varies from day to day. Pain is a predictor of disability and health related quality of life (8).

The magnitude of the long term economic burden of rheumatoid arthritis has previously been underestimated. These patients require long term management to reduce disease progression and to control the frequent flares. Inability to work leads to decreased productivity and early retirement. The patient and the family have to cope with loss of contribution to the society, redefined social roles, low self-esteem, and effects of pain, mental distress, fatigue and depression (9). Criteria for classifying RA is based on the confirmed presence of synovitis in at least one joint and an absence of an alternative explanation for the synovitis. An achievement of a total score of 6 or greater out of 10 from individual scores in four domains that include number and site of joints involved, elevated acute phase response, serological abnormality and the duration of the symptoms. This criterion is important as it puts emphasis on the need for earlier diagnosis and institution of effective disease suppressing therapy. This helps to minimize the occurrence of the undesirable sequalae. Rheumatoid factor is not as specific as anti citrullinated protein antibody for diagnosing RA. Baseline complete blood count is useful in influencing treatment options (1).

Therapeutic intervention should commence as soon as the diagnosis is made with the aim of halting inflammation before irreversible damage sets in (10). Recent guidelines have addressed the management of RA but patient preference is as important. There are specific considerations for special populations because many medications have deleterious effects. The goals of therapy for RA include minimizing joint pain and swelling, preventing deformity, such as, ulnar deviation and radiographic damage, maintaining the quality of life (personal and work) and controlling extra articular manifestations (1). One of the most important aspects of treatment of RA is pain management. Patients suffering from chronic pain or frequent flare ups may benefit from knowing how to manage pain on an ongoing basis and as needed. This greatly improves their quality of life (7). Disease modifying anti rheumatic drugs (DMARDS) are the first line choice of treatment for RA therapy. Non Steroidal Anti inflammatory drugs (NSAIDS) and corticosteroids can be used as short term therapy for controlling pain and inflammation (1).The WHO guidelines for pain relief outlines regular assessment of pain and its severity throughout the course of the disease. It further outlines the use of non-pharmacological measures, administration of analgesic therapy and anticipation and treatment of analgesic side effects. The choice of analgesics

is depended upon pain intensity and the response to previously administered agents. Adjuvant therapy can be used as necessary at any point on the analgesic ladder.

Treatment options for chronic pain fall into various categories. Namely, pharmacologic, physical medicine, behavioral medicine, interventional and surgical approaches. The choice of the therapeutic intervention depends on current medication regimen, prior experience with pain medications, personal experience and fears regarding the use of pain medication, previous use of non-pharmacologic interventions and social and spiritual factors. Combinations of drugs that target different mechanistic pathways may result in improved analgesia and fewer side effects. Comorbidities should be evaluated and treated. If RA is not properly controlled, it can lead to lifetime complications (7).

1.2 Problem statement

Chronic pain can adversely affect a patient's daily living activities that include the ability to work, participate in physical and social activities and general interruption of the day to day life. While the ultimate goal of RA treatment is to suppress disease progression from further damaging joints by sending it into remission, pain management is a necessary daily practice for patients. Despite medications and aggressive forms of treatment, many RA patients experience continuous pain and stiffness (7). Treatment response differs between individuals and no one approach is appropriate for all patients. It is difficult to adequately diagnose or cure pain. Subsequently, the management of pain can be daunting. Few studies evaluating combinations of drugs for chronic rheumatoid pain have been done (11). The increased mortality in these patients is mainly due to accelerated cardiovascular disease especially in those with high disease activity and chronic inflammation. Thus the need to emphasize on earlier diagnosis of RA and immediate initiation of therapy that leads to better prognosis among these patients. The need to reduce, control and prevent rheumatoid pain through proper management of inflammation leads us to the main objective of the study which was to evaluate pain management among patients with rheumatoid arthritis through establishing the types of drugs used, the prevalence of adverse drug reactions encountered, the patient factors impacting pain control and the adequacy of pain control among these patients.

1.3 Study justification

Pain is the most devastating symptom of rheumatoid arthritis and may occur throughout the life of the victim (12). It adversely affects the quality of life especially the physical component leading to disability. The disease impairs activities of daily living, mobility, sleep and rest. It also causes reduced energy and fatigue. Those affected depend on medicinal substances and medical aids to conduct daily activities. The work capacity is significantly reduced. Pain remains a major challenge in the provision of care in rheumatoid arthritis and it's often inadequately controlled (13). The drugs used have several adverse effects which increases the morbidity. Several factors determine how effectively the pain is controlled and it is important therefore to evaluate pain control in order to explore ways of improving its management. The findings of this research will benefit the Kenyatta National Hospital administration, the health care providers and the patients in making informed decisions regarding the management of the disease. This will be accomplished by identifying the knowledge and practice gaps that exists and opportunities for innovative strategies for pain management. Ultimately, the pain burden among those affected will be reduced and their ability to perform daily activities improved leading to enhanced quality of life.

1.4 Objectives

1.4.1 Main objective

To evaluate pain management among patients with rheumatoid arthritis at Kenyatta National Hospital between June and September, 2018.

1.4.2 Specific objectives

1. To find out the types of drugs used to manage pain in rheumatoid arthritis.
2. To determine the prevalence of adverse drug reactions among patients with rheumatoid arthritis.
3. To identify the patient related factors that impact pain control among patients with rheumatoid arthritis.
4. To determine the adequacy of pain control among patients with rheumatoid arthritis.

5. To investigate the determinants of adherence to drugs among patients with rheumatoid arthritis.

1.5 Research questions

1. What types of drugs are used to manage pain in rheumatoid arthritis?
2. What is the prevalence of adverse drug reactions among patients with rheumatoid arthritis?
3. How do patient related factors impact pain control among patients with rheumatoid arthritis?
4. Is pain adequately controlled among patients with rheumatoid arthritis?
5. What are the determinants of adherence to drugs among patients with rheumatoid arthritis?

1.6 Conceptual framework

Figure 1: Conceptual Framework

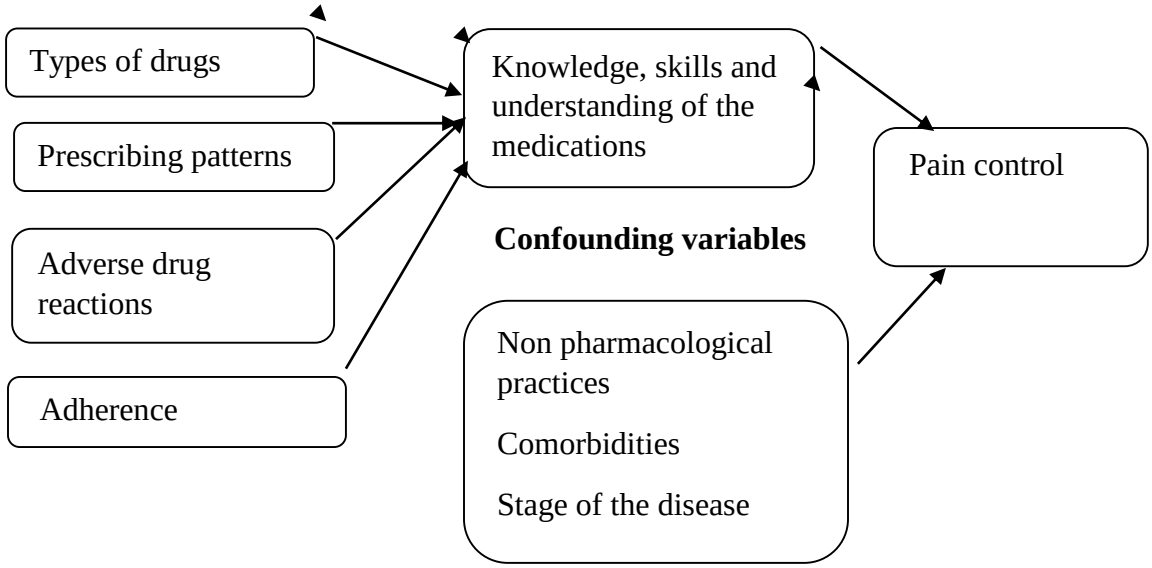

Figure 1: The conceptual framework helps to illustrate the associations between the independent and the dependent variable (Author: Laurine Mukopi,2018).

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

Rheumatology is a discipline that focusses on the care of the patient and management of pain related to the disease (14). Pain is a deleterious symptom experienced by patients with rheumatoid arthritis (RA). They may not be able to avoid it because it can present from the time of diagnosis through the disease progression. It's the inflammatory nature of the disease that causes this unbearable pain. Slowing the disease activity (inflammation) impacts greatly on the amount of pain experienced by the patients and hence their activities of living (15). Chronic pain management necessitates the clinicians to work out a balance between the need for effective pain control and the safety issues associated with the analgesic drugs. RA related pain is not well understood but thought to involve the nociceptive, the non nociceptive and the neuropathic pain mechanisms. The prevailing guidelines do not fully address this nature of pain considering that nociceptive and non nociceptive pain is not differentiated. Management of chronic pain remains a clinical challenge for various reasons. Namely, the progressive nature of the condition, heterogeneity of patient populations, the numerous mechanisms of pain involved, comorbidities, other medications, the efficacy and safety profiles of the available pain medications. Patients with rheumatoid arthritis need pain management therapies that are life long. This rules out those that are unsuitable for continued use but are effective for acute pain. Many pain medications posses a possibility of causing adverse drug reactions prompting the clinicians to under treat the pain in order to minimize the potential ADRs and enhance the safety of the patient. Effective analgesia is actually a human right. Not treating pain is not an option. RA is characterized by flare ups and remissions.The patients may thus endure continuous or intermittent pain which could be of various degrees. This pain can be so intense such that it's triggered by slight movement of the affected joints. The lower thresholds for pressure pain by RA patients suggests an alteration in the central processing of pain while an enhanced cortical response to noxious stimuli suggests cellular changes affecting pain processing signals. The interaction between central sensitization, peripheral sensitization and inflammation are not completely understood among patients with rheumatoid arthritis (14). A review of the types of drugs, their prescribing patterns,

adverse drug reactions, level of adherence and the level of pain control will help in evaluating the management of pain among these patients.

2.2 Types of drugs used for Rheumatoid Arthritis

Various guidelines have addressed the pharmacological management of rheumatoid arthritis putting emphasis on early therapeutic intervention for better prognosis (10). Proper understanding of the underlying pathophysiology of the inflammatory nature of the disease process, the mechanisms of pain and a greater recognition of control of pain have prompted the rheumatologists to contemplate new ways of managing pain. It was suggested that care providers embrace the approach of pain modifying analgesic drugs as opposed to pain control in arthritis related pain (14). The goals of therapy include minimizing joint pain and swelling, preventing deformity, averting extra articular manifestations and maintaining the quality of life.

2.2.1 Disease Modifying Anti Rheumatic Drugs

Disease Modifying Anti Rheumatic Drugs(DMARDs) are the treatment of choice for rheumatoid arthritis (1). The DMARDs can be biologic or non-biologic. The non-biologic (conventional) DMARDs include methotrexate, leflunomide, hydroxychloroquine and sulfasalazine (16). Methotrexate is recommended for active rheumatoid arthritis as the first line treatment of choice unless contraindicated. Leflunomide may be an alternative to Methotrexate or given in combination. Sulfasalazine and hydroxychloroquine are preferred for low disease activity. Combination therapy with two or more DMARDs has been found to be more effective though with more adverse effects. A biologic DMARD can be initiated if rheumatoid arthritis is not well controlled with the non-biologic DMARDs. The biologic DMARDs include Tumor Necrotic Factor inhibitors and interleukin 1 inhibitors. The inhibitors of the Tumour Necrotic Factor are the preferred first lines for biologic therapy. The introduction of TNF alpha antagonists has resulted in considerable progress in the treatment of RA refractory to conventional treatment (17). Use of two or more biologic DMARDs can be considered in case the TNF inhibitors are not effective but the escalated rate of adverse effects would be a source of concern (1).

2.2.2 Corticosteroids

Corticosteroids have potent anti-inflammatory effects thus are effective adjuvant analgesics in RA though the long term adverse effects and toxicity have reduced the clinical benefit of these drugs for long term use. The National Institute for Health and Care Excellence (NICE) guidelines stipulates that patients can only use corticosteroid therapy for extended periods after the long term complications have been fully discussed and all the other treatment options have been offered. Corticosteroids are therefore used for short term management of inflammation in patients with recent onset of RA and disease flares (14).

2.2.3 Analgesics

NSAIDs and COX 2 inhibitors have anti inflammatory, analgesic and anti pyretic activities thus are used to control pain. They are available both on prescription and over the counter. They include diclofenac, ibuprofen, naproxen, ketotifen, celecoxib, meloxicam and piroxicam. NSAIDs are often used without considering their relative contraindications. It's recommended that they are used at the lowest effective dose for the shortest duration of time(14). A proton pump inhibitor should be co prescribed with NSAIDs and COX 2 inhibitors. If the NSAIDs and COX 2 inhibitors do not provide adequate symptom control the DMARDs should be reviewed (18).

Paracetamol has antipyretic and analgesic properties and often considered first line in pain management. Earlier reports indicated that the anti inflammatory activity of Paracetamol is either absent or minimal. More reports indicate that its effect on inflammation could be distinct from the NSAIDs and can be given to RA patients who have inadequate pain control to prevent prolonged use of NSAIDs and COX 2 inhibitors (13). Opioids are recommended for long term non-cancer pain syndromes but there is concern regarding the possibility of addiction. Recent studies have shown that the use of opioids for management of chronic pain conditions are less related to the risk of the development of dependence due to the availability of abuse deterrent formulations (19). Tricyclic antidepressants (TCAs) like amitriptyline provide significant pain relief to RA patients. Anticonvulsants and TCAs are known as pain modifying drugs and have found a wide distribution in arthritis. They offer patients analgesic and antidepressive benefits that include

improvement of fatigue and sleep disorders. Anticonvulsants like gabapentin give pain relief to patients with central sensitization through their mechanism of action. Serotonin Norepinephrine Re uptake inhibitors are not advocated for as first line analgesics for RA patients. They are more tolerated than TCAs but are less effective pain relievers (14). Immunosuppressants can also be used to retard disease progression and thus pain. They include azathioprine, cyclosporin, chlorambucil, cyclophosphamide, tacrolimus and mycophenolate mofetil. Topical agents like capsaicin, diclofenac, salicylate and lidocaine can be used for localized relief of pain. Their benefit is enhanced when used in combination with the systemic agents(14). Other drugs used to manage RA include gold preparations, minocycline, penicillamine and Janus kinase (JAK) inhibitors(20). The multimechanistic nature of RA suggests that combination therapies may be appropriate in providing synergistic analgesic effect and at the same time reduce the side effect profile.

There are slight differences in management of RA depending on the disease state. Patients with newly diagnosed active rheumatoid arthritis, are prescribed methotrexate plus one other DMARD and a short term glucocorticoid ideally within three months of the onset of symptoms. The glucocorticoid can be given orally, intramuscularly or intraarticularly. Patients who have achieved satisfactory levels of disease control, the drug doses can be reduced to levels that can still maintain disease control. The combination DMARD therapy may not be appropriate for some newly diagnosed RA patients. These patients can benefit from monotherapy with attention to fast escalation to a therapeutically effective dose rather than the choice of the DMARD. Doses of DMARDs can be cautiously reduced in patients with established RA whose disease is stable but promptly returned to disease controlling dosages at the first sign of a flare. In case there is need to introduce new drugs to a rheumatoid arthritis patient, consider stopping or decreasing the preexisting rheumatologic drugs once disease is under control(18). Patients with rheumatoid arthritis that is established can only benefit from continued glucocorticoid therapy if all other treatment options have been offered and the long term complications discussed(18).

2.3 Adverse drug reactions associated with drugs used for rheumatoid arthritis

An adverse drug reaction is an unwanted or harmful reaction experienced after the administration of a drug or combination of drugs under normal conditions of use. It may

occur following a single dose or prolonged administration of a drug(21). While all drugs have a potential of causing an adverse drug reaction the patients response varies across the different drugs thus putting the patients in a very vulnerable state. The key drugs used have an immunosuppressant component(22).

2.3.1 Adverse drug reactions associated with DMARDs

A part from increased risk of infections, patients using DMARDS can suffer gastro intestinal irritability exhibiting symptoms such as nausea, vomiting and diarrhea. Methotrexate can further cause abnormal liver function, mouth sores, and shortness of breath, hair loss and chronic cough. It's advisable to co prescribe folate with methotrexate to reduce the adverse effects(20). Leflunomide can damage the liver and cause birth defects that can still happen long after drug is stopped. It's contraindicated in pregnancy and caution should be taken when using on women of reproductive age. Sulfasalazine increases sun sensitivity. Like other DMARDs, TNF inhibitors work by inhibiting certain components of the immune system. Patients should be tested for latent TB and hepatitis B infection before initiation of therapy(20). TNF inhibitors are associated with acute reactions. TNF alpha inhibitors (etanercept and adalimumab) are mostly associated with local reactions but this is not a contraindication to their use. Anaphylaxis and angioedema have also been reported. This emphasizes on the need for close supervision when administering the TNF agents. Acute reactions such as urticaria, bronchospasm, hypotension and tachycardia could be IgE mediated while rubor, chills, chest pain, diaphoresis, nausea and headache are as a result of non-allergic mechanisms. Reduction in the rate of administration and use of acetaminophen and antihistamines may improve signs and symptoms associated with immediate reactions. Severe cases will require the use of corticosteroids, normal saline and adrenaline. A reduction in the incidence of acute reactions has been related to the use of corticosteroids or antihistamines prophylactically. Majority of complications occur between the fourth and sixth administration of the drug (17).

2.3.2 Adverse drug reactions associated with Analgesics

The nociceptive arthritis related pain is effectively managed by NSAIDs though the safety concerns may cause clinicians to under treat this kind of pain. Conventional NSAIDs are

associated with gastro intestinal side effects. NSAIDs and COX 2 inhibitors have been linked to increased cardiovascular risks like heart attack and stroke, especially in high doses (15). NSAIDs may increase blood pressure in hypertensive patients. Increased risk of myocardial infarction is also reported. Non selective NSAIDs can pose gastro intestinal risk at first dose and the use of a PPI does not assure outright protection but co therapy of a selective COX 2 NSAID with a proton pump inhibitor provides prophylaxis against NSAID gastropathy. The incidence of NSAID therapy gastro intestinal adverse events increases with age thus their clinical benefit is limited among the geriatric population. NSAIDs may interact with other medications and therefore caution should be taken when dealing with patients with renal, hepatic and cardiac impairment, asthma, hypertension, SLE, seasonal allergic rhinitis, and mixed connective tissue disorders. Rarely skin is involved. NSAIDs accumulated toxicity make them unsuitable for long term use (14). Paracetamol carries the possibility of hepatotoxicity in high doses. A study showed that paracetamol significantly increased blood pressure in ambulatory patients with coronary artery disease. The frequent use of paracetamol has been linked to an increased risk of hypertension in men. Opioids are appropriate in the management of chronic pain but are associated with adverse events that include; nausea constipation and somnolence. Opiods may be suitable for use in the elderly and at times at low doses. Clinicians should be cautious when prescribing opioids for clinical, legal and public health reasons (14).

Tricyclic antidepressants are associated with sedation, constipation, blurred vision, dizziness and dry mouth. Dry mouth is of particular concern in RA patients with Sjogrens syndrome (23). In patients with ischemic heart disease and ventricular abnormalities, prescribing TCAs with caution is advocated for by the neuropathic pain special interest group. Some TCAs are listed as drugs inappropriate for the geriatric population because of their anticholinergic, sedating and orthostatic hypotension properties and since arthritis mostly occurs in the elderly, TCAs are not among the recommended medications (14). The long term complications of corticosteroids include increased risk of infections, corticosteroid induced osteoporosis and risk of fracture, immunosuppression, weight gain, skin thinning, cushing's syndrome,glaucoma, muscle weakness, onset or worsening of the existing diabetes, hypertension, delayed wound healing and cataracts. Topical agents can cause mild skin irritations though concerns about nerve desensitization caused by capsaicin

being not fully reversible exist and that the risk of skin ulcers in diabetic patients may be increased by the autonomic nerve effects (14).

2.4 Adherence to pain medications

Adherence refers to whether a patient is compliant to the medications given on the prescription. It has been reported in routine clinical practice that adherence to chronic therapy is often suboptimal. Adherence is a crucial component in the evaluation of the effectiveness of a given therapy. Non adherence largely contributes to treatment failure, delayed recovery and progression of disease (16). Non adherence to medications is a common phenomenon among patients but various measures can be initiated to improve it. Some patients do not adhere to drugs because of their unwillingness to complain, multiple comorbidities, atypical pain presentation and decline in cognitive function (24). A study sort to assess the causes of non-adherence among RA patients. It looked at the relative contributors that included age, disability, cognitive function, emotional state, lifestyle and beliefs about illness. The study found that older patients made less adherence errors compared to middle aged adults. Non adherence was predicted by age, a busy lifestyle and cognitive deficits whereas coping with arthritis related moods predicted adherence. No adherence errors were predicted by illness severity, physical function and medication load. Omission of medications conspicuously accounted for most errors. Sufficient cognitive function to manage medications was exhibited by older patients while the middle aged patients were at the greatest risk of mismanaging medications (25). Psychosocial factors play an important role in medication adherence among RA patients. It was found that patients who held stronger beliefs about the necessity of medications predicted higher adherence rates to the medications and surprisingly higher rates were reported among patients with quite a number of medications (25). Adherence to treatment is influenced by beliefs and attitudes towards illness. Most RA patients have positive beliefs about their medications. However, their high level of concern is associated with helplessness and non-adherence. It is estimated that thirty to fifty percent of patients do not adhere to their medications (26). Non adherence barriers should be assessed on an individual basis (27) otherwise can result to unnecessary health costs, changes in treatment, investigations, morbidity and mortality. Identification of RA patients at risk of non-adherence could help in timely interventions (26).

Previous researches have reported that patients with rheumatoid arthritis do not always take NSAIDs as prescribed and prefer taking the drugs in lower doses and less frequently than recommended (27). Analgesics are deemed effective when taken regularly and preemptively to enable continuous pain relief. Methods of assessing compliance include recording the proportion of medications taken, self-reported adherence, assaying drug levels and recording non adherent behaviors though in chronic conditions like arthritis, analgesics may be prescribed to be taken as needed especially where the severity of pain fluctuates. Many RA patients have reported not to be taking their medications before an activity and that they are reluctant to take their pain medications unless unable to tolerate the pain (27). A study found that most RA patients preferred complementary therapy as opposed to conventional treatment. They cited lower incidence of adverse drug reactions, psychological comfort, greater patient choice and an increased quality of patient therapist relationship (28).

2.5 Adequacy of pain control

The rheumatoid arthritis pain is a multimechanistic pain that requires a multidimensional approach in assessing it. Pain scales are of two categories; the single dimensional scales and the multidimensional scales. The single dimensional (unidimensional pain scales) assess a single dimension of pain like pain intensity through patients' self-reporting. They include numerical rating scales, visual analogue scales, verbal rating scales and faces pain rating scales. Multidimensional scales measure intensity, location of pain, nature and impact on patients' mood and activities. The most commonly used tool is the Brief Pain Inventory (BPI) questionnaire (29).

The level of pain control among RA patients will vary depending on the various pain management practices employed by the patients. This include adherence to the pain medications, previous experience with the pain medications, non-pharmacologic interventions, social and spiritual factors (7). A study in journal of pain reported that patients with rheumatoid arthritis experienced barriers to pain management that contributed to poor control of pain. A study that was carried out on sixty RA patients found out that fifty three percent of the patients had moderate to severe pain. Forty seven percent had mild to absent pain while sixty five percent of all participants reported satisfaction with their

current pain control. Eighty percent of the patients were concerned about the side effects of the medications, sixty three percent disliked too many pills, fifty seven percent were concerned about drug interactions, and thirty five percent were worried about addiction, twenty seven percent were concerned about masking the disease. The more the barriers the patients had the higher the pain level. A part from the use of NSAIDs and acetaminophen, patients reported seldom use of other analgesics or other modalities to control pain. RA patients tolerate pain and use limited mechanisms to deal with it (30). Frequent use of analgesics was associated with more pain. This weighted more on patients' beliefs and concerns about medications. Patients with higher scores of self-efficacy reported lower pain intensity and less functional impairment. Self-efficacy here referred to the ability of a patient to manage arthritis and its symptoms (27).

A recent study was performed on RA patients and suggested that there are homogenous subgroups within RA patient populations who differ in the motor pain behavior exhibited. These behaviors include; guarding, active rubbing, bracing, grimacing, sighing and rigidity (30). Patients who have low functional score early in disease, early involvement of many joints, high C reactive protein or erythrocyte sedimentation rate at disease onset, early radiologic changes, positive rheumatoid factor and low socioeconomic status in early stage of disease usually have poor pain and general disease outcomes (31). Unrelieved pain is associated negative consequences such as increased catabolic demands like muscle breakdown, weakness, impaired healing, impaired respiratory effort, inhibited gastrointestinal motility pulmonary and thromboembolic complications and increased sympathetic autonomic stimulation. Persistent pain may lead to a decrease in immune response and psychological effects of anxiety, helplessness and depression (32).

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter describes how the stated objectives were achieved, the type of data, how it was collected and processed. It involves descriptions of the research design, location of the study, study population, sampling technique, research instruments, pre testing, quality assurance, data collection tools, data management, logistical and ethical considerations.

3.2 Research design

A cross sectional survey of the adult patients with a clinical diagnosis of rheumatoid arthritis attending clinic at Kenyatta National Hospital was carried out. This study design was appropriate because of its efficiency and cost effectiveness in providing adequate descriptive and analytic snapshots of population phenomena in a given point in time.

The dependent variable was pain control while the independent variables included types of drugs used for pain management, adverse drug reactions, patient related factors and interefernce with aspects and activities of daily living.

3.3 Location of the study

This study was carried out at Kenyatta National Hospital. It is a tertiary care hospital located to the immediate west of Upper Hill area in Nairobi, the capital and largest city of Kenya. The hospital is approximately 3.5 kilometres from the Central Business District. It is accessible from both Ngong road and Hospital road and lies on 45.7 acres of land. The facility is the largest referral hospital in East and central Africa and also serves as the teaching hospital for the University of Nairobi and the Kenya Medical Training College. It has a bed capacity of 1800 located in 50 wards and 22 outpatient specialized clinics. The hospital employs over 6000 staff (33). This study was particularly carried out at the rheumatology clinic which falls under the medical outpatient clinics in clinic number 17. The patients visit the rheumatology clinic every Thursday and on average, 17 patients with rheumatoid arthritis are reviewed every week. The clinic is staffed by different categories of personnel which includes; records clerks,nurses, medical officer interns, medical officers, registras and consultants. This site was the most appropriate because most patients with rheumatoid arthritis from the wider catchment area, tend to seek services or be referred here to receive treatment for the disease.

3.4 Study population

The study population comprised of adult patients who were eighteen years and above with a clinical diagnosis of rheumatoid arthritis at any stage of disease, on treatment and attending clinic at Kenyatta National Hospital during the study period.

3.4.1 Inclusion criteria

The participants included in the study were:

- Adult patients who were eighteen years and above.
- Having a clinical diagnosis of rheumatoid arthritis.
- On treatment for RA and attending clinic at KNH.
- Those who gave a voluntary informed consent.

3.4.2 Exclusion criteria

The study excluded those paticipants

- Who declined to sign the informed consent form.
- With a clinical diagnosis of rheumatoid arthritis but not on treatment.
- Suffering from mental instability or cognitive impairment.

3.5 Sampling

3.5.1 Sampling technique

The principal investigator used convenient sampling to recruit the study participants. All patients who met the inclusion criteria and gave a voluntary consent were selected from the KNH rheumatology clinic on clinic days (Thursdays) during the study period.

3.5.2 Sample size determination

The prevalence of rheumatoid arthritis is neither known in Kenya nor in the neighboring countries. Nevertheless, there is a study that used seventy six participants and found a lot of similarities in terms of patient characteristics with studies done in Europe and the USA (5). A worldwide estimation of the prevalence of RA is between 0.5 and 1% (3). Now that prevalence was not known, we assumed it was 50% and then used the reduction formula since the sample size was less than 10,000. Sample size was then calculated using The Fisher's formula and then the reduction formula applied as follows:

$$n = \frac{Z^2pq}{d^2}$$

n is the minimum sample size

Z is the standard normal deviate at 95% confidence interval corresponding to 1.96

P is the prevalence of rheumatoid arthritis = 50%

Q is (1- p)

$$n = \frac{1.96^2 (0.5) (0.5)}{0.05^2}$$

$$= \frac{3.8416 \times 0.25}{0.0025}$$

= 384 patients

Average clinic attendance is 136

Using the reduction formula,

$$\frac{n \times N}{n + N}$$

$$= \frac{384 \times 136}{384 + 136}$$

=100

Adjusting for 15% non-response

100 x 1.15

Minimum sample size = 115 patients.

The Kenyatta National Hospital rheumatology clinic receives an average of 17 patients with a clinical diagnosis of rheumatoid arthritis per week. This was per the files perusal for the month of January, 2018. Projecting forward, an average of 136 patients with rheumatoid arthritis would have attended clinic in two months. According to the Fisher's formula above, the sample size used was 115 participants.

3.5.3 Participant recruitment

On the clinic day, the identified patients were comprehensively informed of the study while waiting to be attended to by their physicians. Thereafter, those eligible and willing to volunteer in the study were taken through the consenting process and requested to sign the

consent form (Appendix 2B). Participants were then issued with the questionnaires (Appendix 3, Appendix 4 and Appendix 5), taken through and helped to fill with the support of the Principal Investigator and research assistants. This procedure was repeated on other clinic days until the desired sample size was attained.

To avoid duplicate sampling of the same patient, tags were used after the first encounter. The tags were stapled to the patient files and the date when the participant was seen indicated to ensure they remain in place until the end of the study. No participant was interviewed more than once.

3.6 Research instruments

A screening eligibility form was used to guide the selection of patients who met the inclusion criteria. Informed consent form was used to obtain consent from the patients who met the eligibility criteria. Both the English and Kiswahili versions were available. In case of language barrier proxy consent was obtained from the care giver. A data collection sheet was used to capture patients' characteristics, disease characteristics and management. Structured interviews were performed. Structured questionnaires consisting of the Morisky adherence tool and Brief Pain Inventory questionnaire were administered.

3.6.1 The Morisky adherence tool

The eight item Morisky medication adherence scale was developed from the original four scale Morisky tool and published in 2008. This was an improvement on the four scale tool that had fair psychometric properties and could capture the fundamental reasons for medication underuse or omissions and a bit of disclosures of non-adherence. The first seven items of the modified tool are dichotomous responses with YES or NO and the last item is a five point Likert response. The additional four features try to identify and address the circumstances or situations that are related to the adherence behavior. The MMAS-8 has better psychometric properties with sensitivity and specificity of 93% and 53% respectively and a Cronbach's alpha value of 0.83. It's popular and widely used in various clinical settings and different populations. The tool enjoys higher degree of concordance with pharmacy fill data or electronic monitoring devises. It has less items resulting in less response burden. Medication adherence scales are subjective measures and should be able to accurately capture the beliefs, behaviors and barriers related to medication adherence. It

should be precise, easy to understand and administer (34). For the purpose of this study, a score of more than 2 means low adherence and a score of zero means high adherence on MMAS-8.

3.6.2 The Brief Pain Inventory tool

The Brief Pain Inventory (BPI) is one of the most widely used measurement tools for assessing chronic clinical pain. It allows patients to rate the severity of their pain and the extent to which the pain interferes with various functions. The BPI has been shown to be an appropriate measure of pain caused by varied conditions and thus used in hundreds of studies. It uses four severity items to assess pain; pain at its worst, least, average and current pain. It also measures how much pain has interfered with the seven daily activities including mood, work, and general activity, walking, enjoyment of life, relations with others and sleep. The BPI interference is scored as the mean of the seven interference items. This mean can be used if more than 50% or four of the seven items have been completed on a given administration. In a study of patients with osteoarthritis, the BPI showed a test – retest reliability for pain interference to range from 0.83 to 0.93 beginning at day one for the week. The BPI is a reliable pain assessment tool to the extent that high test – retest reliability and alternate form reliability is demonstrated when pain is stable or when pain changes in a predictable way (35). For the purpose of this study a score of zero means no pain, a score of 1 -3 means mild pain, a score of 4 -7 means moderate pain and a score of 8 – 10 means severe pain.

3.7 Pre testing

The data collection tools were tested on the first ten participants to establish their validity and reliability. External validity was established by choosing an appropriate sample size while internal validity was guaranteed by clear definition of variables. Reliability was checked by testing for the reproducibility of data in the first ten participants. Both the Morisky Medication Adherence Scale-8 (MMAS-8) and the Brief Pain Inventory questionnaire were valid and reliable tools with a Cronbach's alpha coefficient of 0.94 for the BPI and 0.67 (95% confidence interval 0.65 to 0.69) for MMAS-8 (36) (37).

3.8 Data collection techniques

A Data collection sheet that captured the patients' characteristics, disease characteristics and management was used. Structured interviews were conducted on patients. The investigator administered and filled the Morisky Medication Adherence Scale-8 to assess adherence and Brief Pain Inventory Questionnaire to assess the level of pain control. The investigator checked the patients' files for drugs, laboratory and diagnosis information.

3.9 Data management

Data was collected using structured and standardized tools. It was stored in password protected Microsoft excel. Confidentiality was ensured by use of unique identifiers for the forms used to retrieve data from the files. All documents linking the collected data to the patients' files were stored under lock and key and only accessible to the principle investigator, supervisors and the regulatory team. All data collected was coded, cleaned, processed, recorded and stored in a way that allowed accurate reporting, interpretation and verification. Data entry was backed up every often and after completion of study all data was disposed. Summary statistics including calculation of means and ranges was done on the data collected. Frequency distribution tables were constructed and data was presented in form of bar graphs, pie charts, histograms and percentages. Measures of occurrence including point prevalence and odds were used to analyze the occurrence of adverse drug reactions. Inferential statistics was used to analyze the data collected on all the objectives. *P* values, Confidence intervals, odds ratios and logistic regression modelling was used. These statistics established the relationship between the outcome and a set of covariates and helped to find out the most important predictor of the outcome. The *P* value was set at a significance level of 0.05. Values less than 0.05 were considered statistically significant. The confidence intervals were set at 95%.

3.10 Ethical and logistical considerations

Ethical approval was sought from the KNH/UON Research and Ethics Review Committee whereas authorization to carry out the study was sought from the Kenyatta National Hospital administration and also from the head of the department of the rheumatology clinic at Kenyatta National Hospital before starting the study. Voluntary consent was sought from the participants and only those who gave a voluntary consent were recruited

to the study. The study was fully explained to the participants, their concerns addressed including upholding confidentiality and they were at liberty to leave the study at any time. Their departure was not prejudized or penalized in any way.

CHAPTER FOUR: RESULTS

4.1 Social demographic data

A total of 115 participants were recruited to the study. The male and female representation was skewed with a female preponderance (n = 103, 89.8%) **(Table 1).** The mean age was 48 years old with a standard deviation of 16.4 while the range was 18 to 83 years.

Table 1: Socio Demographic characteristics

Variable	Category	Frequency, n	Percentage, %
Sex	Male	12	10.4
	Female	103	89.6
Age (years)	18 – 35	29	25.2
	36 - 55	44	38.3
	56 - 64	20	17.4
	65 and above	22	19.1
BMI	Below 18.5	5	4.4
	18.5 – 25	43	37.4
	25.5 – 30	51	44.4
	Above 30	16	13.9
Marital status	Single	44	38.3
	Married	71	61.7
Employment status	Unemployed	83	72.2
	Employed	32	27.8
Education status	None	6	5.2
	Primary	31	27.0
	Secondary	49	42.6
	Tertiary	29	25.2
Religion	Christian	115	100
Alcohol intake	Yes	5	4.4
Smoking	Yes	3	2.6
Regular exercise	Yes	87	75.7

Majority (n = 51, 44.4%) of the participants were overweight followed closely by those who had an ideal body weight (n = 43, 37.4%).

Seventy one (61.7%) participants were married. Those who claimed to be unemployed were 72.2%. Almost all participants had a formal education with those who attended secondary school recording the highest at 49 (42.6%). Majority (n = 87, 75.7%) of the participants reported participating in various aspects of regular exercises. Alcohol intake and smoking recorded the lowest participation at 5 (4.4%) and 3 (2.6%) respectively**.**

4.2 Classes of drugs prescribed

DMARDS were the most prescribed class of drugs at 111 (96.5%) as shown in **Figure 2**. Analgesics, folic acid, proton pump inhibitors, corticosteroids and calcium supplements also had a considerable presence on the prescriptions with over forty percent representation.

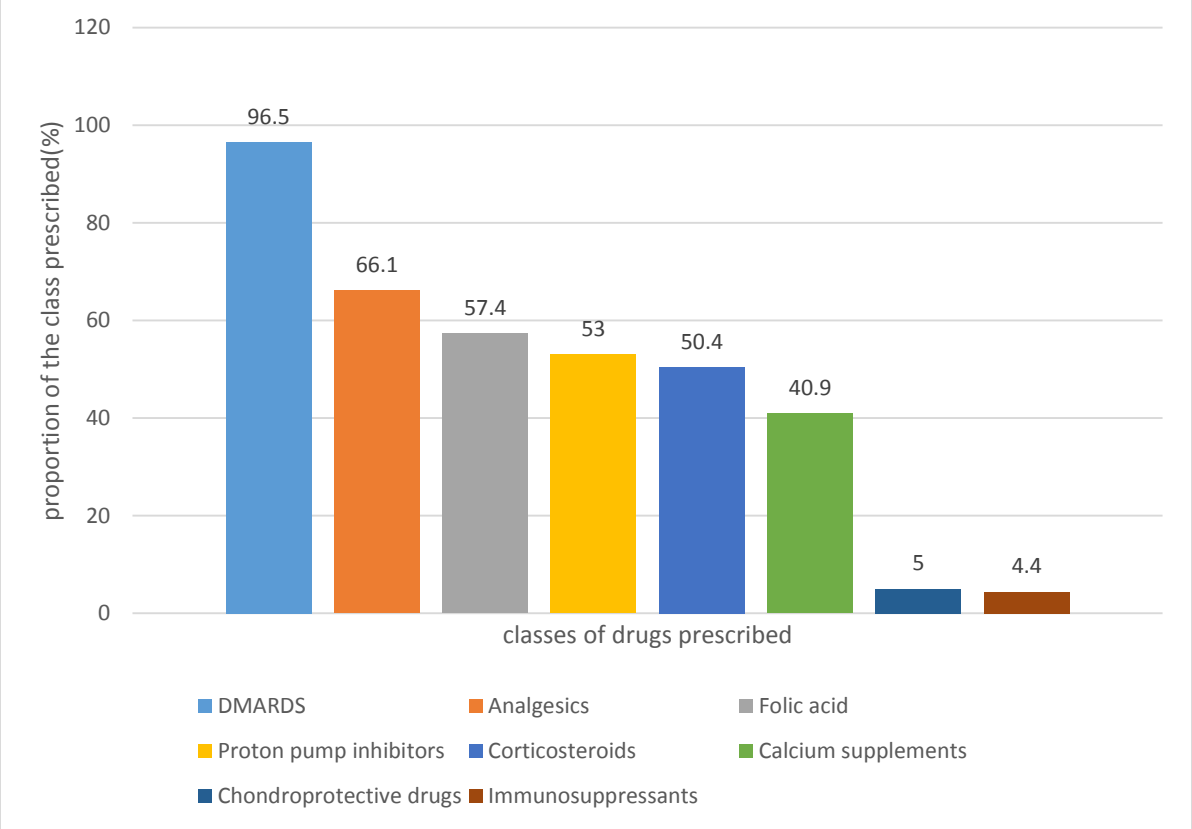

Figure 2:Classes of drugs prescribed

4.3 Drugs used to manage rheumatoid arthritis

The most prescribed DMARDs were methotrexate at 74 (64.4%) and hydroxychloroquine at 50 (43.5%) as shown in **table 2**. Twenty seven (23.5%) participants used leflunomide while only twelve (10.4%) used sulfasalazine. Very few participants were on an immunosuppressant (azathioprine). Fifty (43.5%) participants were on prednisolone. Betamethasone dipropionate/betamethasone disodium phosphate (diprofos) was the least prescribed corticosteroid (n = 3, 2.6%). Twenty nine (25.2%) participants used meloxicam

while 18 (15.7%) used celecoxib as their analgesic. The proportion of the other analgesics used was below 10%. Forty six (40%) participants were prescribed for a calcium supplement while more than half of the participants had folic acid on their prescriptions (n = 66, 57.4%). Omeprazole (n = 47, 40.9%) was the most prescribed proton pump inhibitor. Very few prescriptions had pantoprazole as the preferred proton pump inhibitor at 6 (5.2%). The chondroprotective drugs appeared the least on the prescriptions (n = 6, 5.2%). Topical NSAIDs were not used as much as only 4 (3.5%) participants had them on their prescriptions.

Table 2. Specific drugs used to manage rheumatoid arthritis

Variable (Drug name)	Frequency , n	Percentage, %
Methotrexate	74	64.4
Folic acid	66	57.4
Hydroxychloroquine	50	43.5
Prednisolone	50	43.5
Omeprazole	47	40.9
Calcium supplements	46	40
Meloxicam	29	25.2
Leflunomide	27	23.5
Celecoxib	18	15.7
Drugs for neuropathic pain	17	14.8
Sulfasalazine	12	10.4
Etoricoxib	10	8.7
Aceclofenac	10	8.7
Esomeprazole	8	7
Deflazacort (yescort)	6	5.2
Aceclofenac/Paracetamol	6	5.2
Chondroprotective drugs	6	5.2
Pantoprazole	6	5.2
Azathioprine	4	3.5
Topical NSAIDs	4	3.5
Betamethasone dipropionate/betamethasone disodium phosphate (diprofos)	3	2.6
Aceclofenac/Paracetamol/chlorzoxazone	2	1.7
Chlorzoxazone/Paracetamol (myolgin)	2	1.7
Tramadol	2	1.7
Others	1	0.9

4.4 Comorbidities

Sixty four (55.6%) participants did not report any comorbidity **(Figure 3).** However, hypertension was the highest recorded comorbidity at 41 (35.7%). Each of the other reported comorbidities had less than 10% involvement. Diabetes mellitus and systemic lupus erythematosus had 4 (3.5%) participants each. Three (2.6%) participants had deep venous thrombosis. Two (1.7%) of the participants each had Asthma, H.IV, osteoarthritis, varicose veins, and hemorrhoids. The other seven comorbidities had a single (0.9%) participant each. They included neurofibromatosis, hypothyroidism, lumber spondylitis, Sjogrens syndrome, sciatica and prostate hypertrophy.

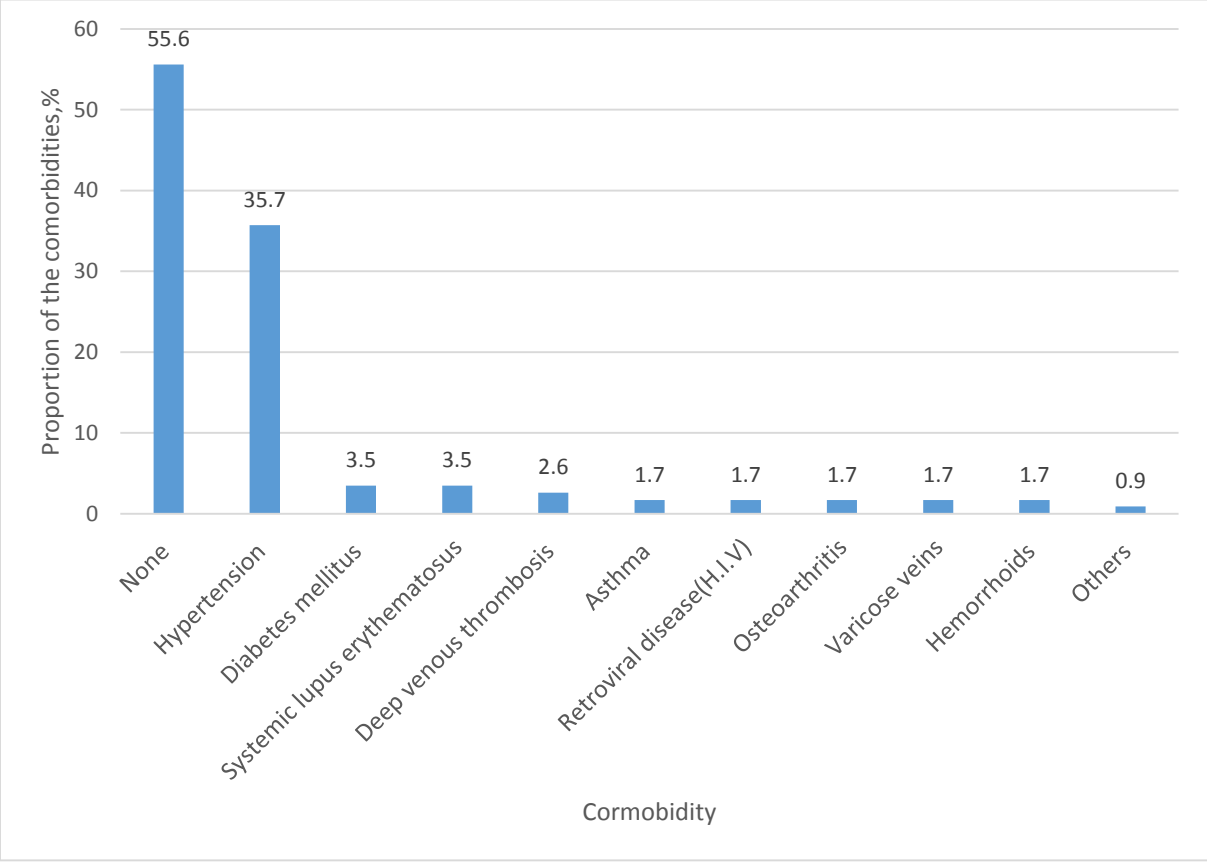

Figure 3: Comorbidities

4.5 Drugs used to manage comorbidities

The most prescribed antihypertensive was losartan H at 13 (11.3%) followed by amlodipine (n = 10, 8.7%) and nifedipine (n = 9, 7.8%) as shown in **table 3.** Aldactone was the least

prescribed anti-hypertensive. The diabetic patients used metformin (n = 3, 2.6%) and mixtard insulin (n = 1, 0.9%). Deep venous thrombosis was managed by warfarin (n = 3, 2.6%) and rivaroxaban (n = 1, 0.9%). The asthmatic patients used symbicort (n = 2, 1.7%).

Table 3. Types of drugs prescribed to treat the comorbidities

Variable (drug name)	Frequency, n	Percentage, %
Losartan H	13	11.3
Amlodipine	10	8.7
Nifedipine	9	7.8
Losartan	8	7
Enalapril	4	3.5
Carvedilol	4	3.5
Hydrochlorthiazide	3	2.6
Nebivolol	3	2.6
Metformin	3	2.6
Warfarin	3	2.6
Aldactone	2	1.7
Budesonide/formoterol fumarate (symbicort)	2	1.7
Daflon	2	1.7
Lactulose	2	1.7
Others	1	0.9

4.6 Adverse Drug Reactions

Participants reported various adverse drug reactions **(Table 4).** Abdominal pain and headache were the most reported adverse drug reactions at a frequency of 16 (13.9%) and 14 (12.2%) respectively. Eleven (9.6%) participants revealed that they felt fatigued after taking the medications. Nausea and peptic ulcers afflicted 10 (8.7%) participants each. Pruritus and back pain was each reported by 7 (6.1%) participants after using the medications. Six (5.2%) participants had insomnia while six (5.2%) others reported coughing. Vomiting, mucositis and corneal changes were each revealed by 5 (4.4%)

participants. Four (3.5%) respondents suffered from respiratory infections and increase in blood pressure was reported by three (2.6%) of them. Only two (1.7%) participants experienced epigastric pain after taking the medications.

Table 4. Prevalence of adverse effects

Variable (ADR)	Frequency (n)	Percentage (%)
Abdominal pain	16	13.9
Headache	14	12.2
Fatigue	11	9.6
Nausea	10	8.7
Peptic ulcers	10	8.7
Pruritus	7	6.1
Back pain	7	6.1
Cough	6	5.2
Insomnia	6	5.2
Vomiting	5	4.4
Mucositis	5	4.4
Corneal changes	5	4.4
Respiratory infections	4	3.5
Dizziness	4	3.5
Anorexia	3	2.6
Fever	3	2.6
Increased blood pressure	3	2.6
Weight loss	2	1.7
Urticaria	2	1.7
Night sweats	2	1.7
Epigastric pain	2	1.7
Constipation	2	1.7
Others	1	0.9

4.7 Inflammation markers

Erythrocyte sedimentation rate and C reactive protein were the inflammation markers used to diagnose the disease and monitor therapy. All participants who had their markers checked presented a similar distribution pattern where both markers were either high or normal. Most participants had both high ESR and CRP at 36 (75%) as shown in **Figure 4.**

Inflammation markers

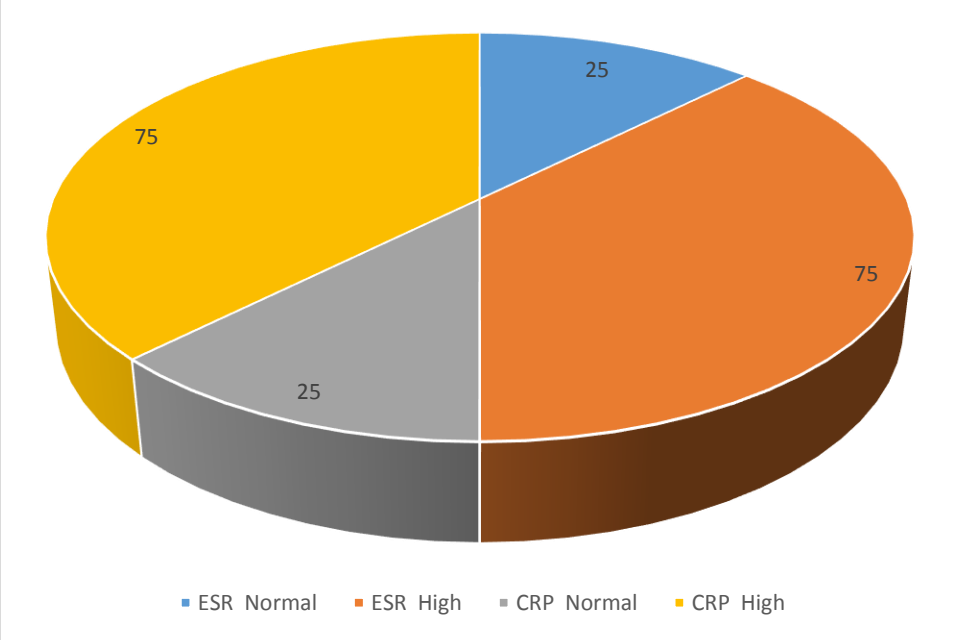

Figure 4: Inflammation markers

4.8 Adherence to drugs for rheumatoid arthritis

For the purpose of this study, a score of 2 or more meant low adherence and a score of zero meant high adherence on MMAS-8. Eighty three (72.2%) participants had low adherence to medications while 32 (27.8%) had high adherence **(Figure 5).**

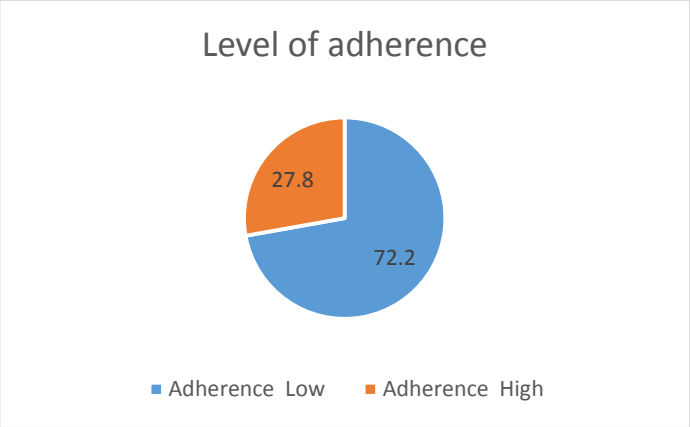

Figure 5. Level of adherence to medicines

The reasons for non-adherence were categorized as patient related, hospital related, therapy related, condition related as well as socioeconomic factors **(Figure 6).** Social and economic factors were the predominant at 82 (71.3%) followed by patient related factors (n = 68, 59.1%).

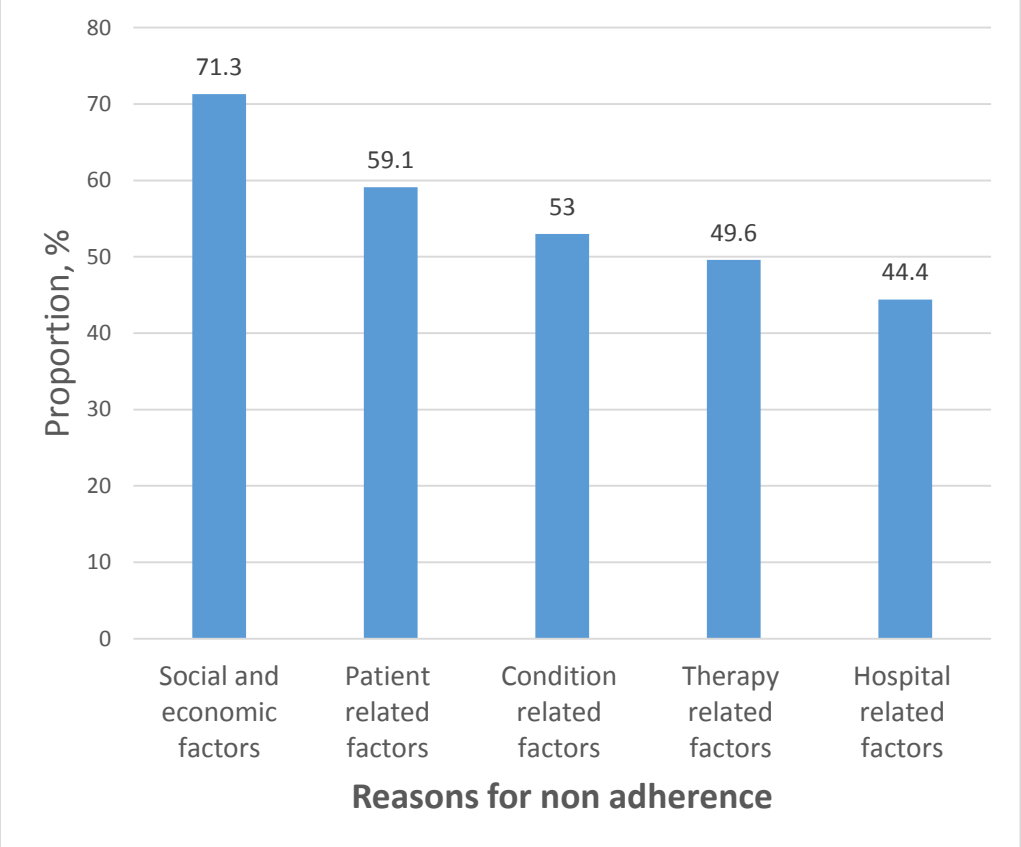

Figure 6. Reasons for non-adherence

Fifty one (44.4%) participants cited hospital related factors as some of their reasons for non-adherence to medications **(table 5).**

Table 5: Reasons for non- adherence to medicines

Variable	Frequency, n	Percentage, %
Social and economic factors		
Lack of finances	81	70.4
Inadequate knowledge of treatment	13	11.3
Culture and believes about illness	6	5.2
Family dysfunction	2	1.7
Condition related factors		
Severity of the disease	59	51.3
Level of disability	21	18.3
Availability of effective treatments	6	5.2
Therapy related factors		
Duration of treatment	54	47.0
Adverse drug reactions	41	35.7
Complexity of the medical regimen	15	13.0
Frequent changes in treatment	6	5.3
Patient related factors		
Forgetfulness	60	52.2
Did not know I had to take drugs daily	43	37.4
Anxiety of possible adverse effects	43	37.4
Misunderstanding of treatment instructions	18	15.7
Fear of dependence	8	7.0
Hospital related factors		
Drug is unaffordable	50	43.5
Drug unavailable in pharmacy	28	24.4
Instructions not clear	15	13.0
Concerns not addressed	4	3.5

Majority (n = 81, 70.4%) of the participants revealed that lack of finances was their major reason for non-adherence and 13 (11.3%) cited inadequate knowledge of treatments. Severity of disease was the main condition related factor that affected adherence at 59 (51.3%) followed by disability at 21 (18.3%). Fifty four (47%) participants disclosed that the long duration of treatment was their main therapy related factor that interfered with

their adherence to medications. The anxiety of developing an adverse drug reaction was reported by 41 (35.7%) participants.

Sixty (52.2%) participants stated that forgetfulness was their hindrance to adherence while 43 (37.4%) were not aware that they had to take some of the drugs daily. Further, fifty (43.5%) participants said that their medications were unaffordable while twenty eight (24.4%) insinuated that the drugs were unavailable in the hospital pharmacy.

4.9 Evaluation of pain

For the purpose of this study a score of zero meant no pain, a score of 1 -3 meant mild pain, a score of 4 -7 meant moderate pain and a score of 8 – 10 meant severe pain. Majority (n = 93, 80.9%) of the participants were experiencing pain on the day of the interview. About half (n = 48, 51.6%) of them had severe pain while twenty six (28%) reported mild pain **(Table 6).**

Table 6: Pain evaluation

Variable	Category	Frequency , n	Percentage ,%
Joint pain	Yes	93	80.9
Pain description	Severe	48	51.6
	Mild	26	28
	Moderate	19	20.4

Fifty three (46.1%) participants reported severe pain as the worst level of pain felt in their previous week. Only ten (8.7%) participants reported no pain in their previous week. Further, close to half (n = 51, 44.4%) of the participants reported severe pain as their average level of pain felt. **(Table 7).**

Table 7: Pain evaluation in the past week (Brief Pain Inventory tool)

Variable	Category	Frequency, n	Percentage, %
Worst	Severe	53	46.1
	Moderate	29	25.2
	Mild	23	20.0
	No pain	10	8.7
Least	Severe	48	41.7
	Mild	30	26.1
	Moderate	26	22.6
	No pain	11	9.6
Average	Severe	51	44.4
	Mild	38	33.0
	Moderate	21	18.3
	No pain	5	4.4
Pain now	Severe	45	39.1
	Mild	33	28.7
	Moderate	22	19.1
	No pain	15	13.0
Relief from pain medication	80%	35	30.4
	70%	30	26.1
	90%	18	15.7
	60%	16	13.9
	100%	6	5.2
	50%	5	4.4
	40%	3	2.6
	30%	2	1.7

Thirty five (30.4%) participants revealed that their medications gave them eighty percent relief. This was followed closely by 30 (26.1%) participants who pointed out that their medications gave them 70% relief from pain. Six (5.2%) participants had no doubt that

their medications gave them 100% relief. However, two (1.7%) participants expressed dissatisfaction by their medications claiming they only gave them 30% relief.

4.10 Interference with the activities of daily living

It was noted that most aspects and activities of daily living among the patients with rheumatoid arthritis were interfered with by pain at various levels **(Table 8).**

Table 8: Interference with the activities of daily living

Variable	Category	Frequency, n	Percentage, %
General activity	High interference	83	72.2
	Low interference	27	23.5
	No interference	5	4.3
Mood	High interference	47	40.9
	Low interference	36	31.3
	No interference	32	27.8
Walking ability	High interference	78	67.8
	Low interference	29	25.2
	No interference	7	6.1
Normal work	High interference	85	73.9
	Low interference	24	20.9
	No interference	6	5.2
Relations with other people	Low interference	51	44.3
	No interference	33	28.7
	High interference	31	27.0
Sleep	High interference	62	53.9
	Low interference	37	32.2
	No interference	16	13.9
Enjoyment of life	Low interference	52	45.2
	High interference	47	40.9
	No interference	16	13.9

Normal work being the most interfered with at 85 (73.9%) while relations with other people being the least interfered with. There was considerable interference with the general

activity (n = 83, 72.2%), walking ability (n = 78, 67.8%), sleep (n = 62, 53.9%) and mood (n = 47, 40.9%).

4.11 Bivariate analysis between adequacy of pain control and other variables

4.11.1 Association between social demographic characteristics and pain

The association between sociodemographic characteristics and pain control was determined using Fischer's exact test and the results are shown in **table 9**. The employment status was found to be significantly associated with the adequacy of pain control (*P* = 0.039). More of the employed participants (n = 4, 12.5%) reported no pain as compared to the unemployed participants (n = 1, 1.2%). Moreover, majority (n = 41, 49.4%) of the unemployed participants reported severe pain compared to 10 (31.3%) of the employed ones. The other factors including sex, age category, body mass index, marital status, education level and whether they participated in regular exercises or not were not significantly associated with the adequacy of pain control.

Table 9: Association between sociodemographics and adequacy of pain control

Variable	Adequacy of pain control				*P* value
	No pain n (%)	Mild pain n (%)	Moderate pain n (%)	Severe pain n (%)	
Sex					1.000
Male	0 (0)	4 (33.3)	2 (16.7)	6 (50)	
Female	5 (4.9)	34 (33)	19 (18.4)	45 (43.7)	
Age category(years)					0.633
18 -35	2 (6.9)	10 (34.5)	5 (17.2)	12 (41.4)	
36 -55	3 (6.8)	11 (25)	7 (15.9)	23 (52.3)	
56 -64	0 (0)	10 (50)	3 (15)	7 (35)	
65 years and above	0 (0)	7 (31.8)	6 (27.3)	9 (40.9)	
BMI					0.854
Below 18.5	1 (20)	2 (40)	0 (0)	2 (40)	
18.5 -25	1 (2.3)	15 (34.9)	7 (16.3)	20 (46.5)	
25.5 – 30	2 (3.9)	16 (31.4)	11 (21.6)	22 (43.1)	
Above 30	1 (6.3)	5 (31.3)	3 (18.8)	7 (43.8)	
Marital status					0.388
Single	0 (0)	16 (36.4)	8 (18.2)	20 (45.5)	
Married	5 (7)	22 (31)	13 (18.3)	31 (43.7)	
Employment status					**0.039***
Unemployed	1 (1.2)	27 (32.5)	14 (16.9)	41 (49.4)	
Employed	4 (12.5)	11 (34.4)	7 (21.9)	10 (31.3)	
Education status					0.459
None	0 (0)	2 (33.3)	2 (33.3)	2 (33.3)	
Primary	0 (0)	10 (32.3)	5 (16.1)	16 (51.6)	
Secondary	3 (6.1)	13 (26.5)	8 (16.3)	25 (51)	
Tertiary	2(6.9)	13 (44.8)	6 (20.7)	8 (27.6)	
Alcohol intake					0.604
Yes (n = 5)	0 (0)	1 (20)	2 (40)	2 (40)	
Smoking					1.000
Yes (n = 3)	0 (0)	1 (33.3)	0 (0)	2 (66.7)	
Regular exercises					0.224
Yes (n = 87)	5 (5.7)	32 (36.8)	15 (17.2)	35 (40.2)	

**-Statistically significant p value*

4.11.2 Classes of drugs and adequacy of pain control

The association between classes of drugs and pain control was determined using Fischer's exact test and the results are shown in **table 10**. Immunosuppressants were found to be significantly associated with adequacy of pain control (P = 0.033). No patient on an immunosuppressant reported severe pain. Folic acid was mostly prescribed with methotrexate and was also found to be significantly associated with adequacy of pain control (P = 0.049). Four (6.1%) participants on folic acid reported no pain. Participants on DMARDs were more likely to report no pain (5, 4.5%) . Other classes of drugs that included corticosteroids, analgesics, calcium supplements, proton pump inhibitors and chondroprotective medicines were not significantly associated with adequacy of pain control.

Table 10: Association between classes of drugs prescribed and pain control

Variable	**Adequacy of pain control**				***P* value**
	No pain n (%)	**Mild pain n (%)**	**Moderate pain n (%)**	**Severe pain n (%)**	
DMARDS (n = 111)	5 (4.5)	38 (34.2)	19 (17.1)	49 (44.1)	0.315
Immunosuppressants(n = 5)	1 (20)	2 (40)	2 (40)	0 (0)	**0.033***
Corticosteroids (n = 58)	4 (6.9)	18 (31)	12 (20.7)	24 (41.4)	0.513
Analgesics (n = 76)	2 (2.6)	20 (26.3)	15 (19.7)	39 (51.3)	0.055
Calcium supplements(n = 47)	1 (2.1)	17 (36.2)	10 (21.3)	19 (40.4)	0.631
Proton pump inhibitors (n = 61)	3 (4.9)	18 (29.5)	11 (18)	29 (47.5)	0.824
Folic acid (n = 66)	4 (6.1)	26 (39.4)	7 (10.6)	29 (43.9)	**0.049***
Chondroprotective meds (n = 6)	0 (0)	0 (0)	1 (16.7)	5 (83.3)	0.196

*-*statistically significant p value*

4.11.3 Adverse drug reactions and adequacy of pain control

The association between adverse drug reactions and pain control was determined using Fischer's exact test and the results are shown in **table 11**. Participants who experienced fatigue after

Table 11: Relationship between adverse drug reactions and adequacy of pain control

Variable	Adequacy of pain control				*P* value
	No pain	Mild pain	Moderate pain	Severe pain	
Nausea (n = 10)	0 (0)	2 (20)	0 (0)	8 (80)	0.151
Vomiting (n = 5)	0 (0)	2 (40)	0 (0)	3 (60)	0.769
Pruritus (n = 7)	0 (0)	2 (28.6)	3 (42.9)	2 (28.6)	0.420
Abdominal(n = 16) pain	0 (0)	3 (18.8)	4 (25)	9 (56.3)	0.439
Fatigue (n = 11)	0 (0)	0 (0)	3 (27.3)	8 (72.7)	**0.036***
Cough(n = 7)	0 (0)	1 (14.3)	2 (28.6)	4 (57.1)	0.662
Back pain (n = 7)	0 (0)	3 (42.9)	0 (0)	4 (57.1)	0.710
Dizziness (n = 4)	0 (0)	0 (0)	0 (0)	4 (100)	0.277
Increased blood pressure(n = 3)	0 (0)	1 (33.3)	2 (66.7)	0 (0)	0.124
Constipation (n = 2)	0 (0)	1 (50)	1 (50)	0 (0)	0.346

**-statistically significant p value*

taking the medications had either moderate (n = 3, 27.3%) or severe pain (n = 8, 72.7%) and the association was statistically significant (*P* = 0.036). The other adverse drug reactions experienced by the participants were not significantly associated with adequacy of pain control.

4.11.4 Social and economic factors and pain control

The association between the socioeconomic factors and pain control was determined using Fischer's exact test and the results are shown in **table 12**. No significant association was found between these factors and pain control. All the factors namely, lack of finances, culture and beliefs about illness, family dysfunction and inadequate knowledge of treatment posted *P* values that were more than 0.05. Forty (49.4%) participants who

revealed that lack of finances interfered with their adherence to medications reported severe pain.

Table 12: Association between Socioeconomic factors and pain control

Variable	Adequacy of pain control				*P* value
	No pain n (%)	**Mild pain n (%)**	**Moderate pain n (%)**	**Severe pain n (%)**	
Lack of finances (n = 81)	3 (3.7)	22 (27.2)	16 (19.8)	40 (49.4)	0.153
Culture and beliefs (n = 6)	0 (0)	1 (16.7)	1 (16.7)	4 (66.7)	0.810
Family dysfunction (n = 2)	0 (0)	0 (0)	1 (50)	1 (50)	0.515
Inadequate knowledge of treatment (n = 13)	0 (0)	2 (15.4)	1 (7.7)	10 (76.9)	0.135

4.11.5 Therapy related factors and pain control

The association between therapy related factors and pain control was determined using Fischer's exact test and the results are shown in **table 13**. There was a significant association between occurrence of an adverse drug reaction and adequacy of pain control (*P*=0.050). None of the participants with an adverse drug reaction reported no pain while

Table 13: Therapy related factors and adequacy of pain control

Variable	Adequacy of pain control				*P* value
	No pain n (%)	**Mild pain n (%)**	**Moderate pain n (%)**	**Severe pain n (%)**	
Level of disability (n = 21)	0 (0)	5 (23.8)	5 (23.8)	11 (52.4)	0.562
Severity of the disease (n = 59)	1 (1.69)	17 (28.8)	11 (18.6)	30 (50.8)	0.294
Duration of treatment(n = 54)	0 (0)	15 (27.8)	13 (24.1)	26 (48.1)	0.055
Complexity of the medical regimen (n = 15)	0 (0)	5 (33.3)	4 (26.7)	6 (40)	0.784
Frequent changes in treatment(n = 6)	0 (0)	2 (33.3)	2 (33.3)	2 (33.3)	0.607
Adverse drug reactions(n = 41)	0 (0)	9 (22)	10 (24.4)	22 (53.6)	**0.050***
Did not know had to take drugs daily(n = 43)	0 (0)	10 (23.3)	9 (20.9)	24 (55.8)	0.063
Forgetfulness (n = 60)	1 (1.7)	15 (25)	14 (23.3)	30 (50)	0.064
Anxiety of possible adverse effects(n = 43)	0 (0)	9 (20.9)	10 (23.3)	24 (55.8)	**0.028***
Misunderstanding of treatment instructions (n = 180)	0 (0)	4 (22.2)	3 (16.7)	11 (61.1)	0.496

**-statistically significant p value*

more than half (n = 22, 53.6%) had severe pain. All participants who were anxious about developing an adverse drug reaction experienced pain to some extent while twenty four (55.8%) had severe pain and this relationship was significant (*P* = 0.028). Twenty four (55.8%) participants who did not know they had to take drugs daily reported experiencing severe pain though the relationship was not significant. Half of the participants who occasionally forgot to take their medications as required and those who intimated that the duration of treatment was long experienced severe pain.

4.11.6 Hospital related factors and pain control

The association between the hospital related factors and pain control was determined using Fischer's exact test and the results are shown in **table 14.** Hospital related factors were not significantly associated with the adequacy of pain control. They included unavailability of drugs in the hospital pharmacy, drug unaffordability and unclear instructions for the medications given. They all posted *P* values that were more than 0.05. Fourteen (50%) participants who revealed that the drugs were not available in the hospital pharmacy had severe pain.

Table 14: Hospital related factors and adequacy of pain control

Variable	**Adequacy of pain control**				***P* value**
	No pain	**Mild pain**	**Moderate pain**	**Severe pain**	
Drug unavailable in the pharmacy(n = 28)	0 (0)	7 (25)	7 (25)	14 (50)	0.370
Drug is unaffordable (n = 50)	0 (0)	14 (28)	12 (24)	24 (48)	0.096
Instructions not clear(n = 15)	0 (0)	3 (20)	3 (20)	9 (60)	0.546

4.11.7 Pain and interference with activities of daily living

The association between pain and interference with activities of daily living was determined using Fischer's exact test and the results are shown in **table 15.** There was a significant relationship between pain and interference with the participants' moods ($P = 0.003$). For the participants who reported no interference three (9.4%) had no pain but for those who reported high interference only one (2.1%) had no pain. Interference with the ability to walk was significantly associated with pain control ($P < 0.001$). For the participants who said they had no interference with their ability to walk, none of them had severe pain. All those participants who disclosed that pain interfered with their ability to walk experienced it to some extent. More than half of the participants who said that pain caused high interference

Table 15: Association between pain control and activities of daily living

Variable	Adequacy of pain control				*P* value
	No pain n (%)	**Mild pain n (%)**	**Moderate pain n (%)**	**Severe pain n (%)**	
Mood					**0.003***
No interference	3 (9.4)	17 (53.1)	4 (12.5)	8 (25)	
Low interference	1 (2.7)	14 (38.9)	7 (19.4)	14 (38.9)	
High interference	1 (2.1)	7 (14.9)	10 (21.3)	29 (61.7)	
Normal work					**< 0.001***
No interference	1 (16.7)	5 (83.3)	0 (0)	0 (0)	
Low interference	3 (12.5)	17 (70.8)	2 (8.3)	2 (8.3)	
High interference	1 (1.2)	16 (18.8)	19 (22.4)	49 (57.6)	
Relations with other people					0.213
No interference	2 (6.1)	16 (48.5)	3 (9.1)	12 (36.4)	
Low interference	2 (3.9)	16 (31.4)	10 (19.6)	23 (45.1)	
High interference	1 (3.2)	6 (19.4)	8 (25.8)	16 (51.6)	
Sleep					**< 0.001***
No interference	1 (6.3)	5 (31.3)	3 (18.8)	7 (43.8)	
Low interference	3 (8.1)	22 (59.5)	4 (10.8)	8 (21.6)	
High interference	1 (1.6)	11 (17.7)	14 (22.6)	36 (58.1)	
Enjoyment of life					**< 0.001***
No interference	3 (18.8)	8 (50)	2 (12.5)	3 (18.8)	
Low interference	2 (3.8)	26 (50)	6 (11.5)	18 (34.6)	
High interference	0 (0)	4 (8.5)	13 (27.7)	30 (63.8)	

**- statistically significant p value*

with their normal work reported severe pain (n = 49, 57.6%) while those who denied any interference with their normal work none reported severe pain (0,0%). This association was significant ($P < 0.001$). Sleep was significantly associated with adequacy of pain control ($P < 0.001$) where those who could hardly sleep experienced severe pain. Enjoyment of life and pain control were significantly associated ($P < 0.001$). All the participants who stated high interference with their enjoyment of life felt pain.

4.11.8 Predictors of adequacy of pain control

Logistic regression analysis was carried out to determine the predictors of pain control. The level of pain control was the dependent variable while other factors were independent variables and the results are shown in **table 16**.

Table 16: Logistic regression of predictors of pain control

Variable	Bivariate analysis	*P* value	Multivariate analysis	*P* value
	COR (95%CI)		**AOR (95%CI)**	
Age	1.019 (0.965-1.077)	0.497	0.945 (0.844-1.058)	0.329
Employment status	0.085 (0.009-0.796)	**0.031***	0.093 (0.008-1.119)	0.061
Education status	0.409 (0.113-1.481)	0.173	0.314 (0.043-2.270)	0.251
Immunosuppressants	0.150 (0.14-1.677)	0.124	0.198 (0.010-3.650)	0.277
Corticosteroids	0.241 (0.026-2.226)	0.210	0.229 (0.015-3.318)	0.280
Analgesics	3.083 (0.493-19.279)	0.229	6.859 (0.619-76.013)	0.117
Folic acid	0.323 (0.035-2.983)	0.319	0.150 (0.122-1.835)	0.287
Lack of finances	1.625 (0.259-10.189)	0.604	1.672 (0.254-10.980)	0.592
Severity of the disease	4.461 (0.483-41.204)	0.187	0.564 (0.047-6.751)	0.651
Forgetfulness	4.627 (0.501-42.739)	0.177	0.395 (0.031-4.958)	0.472
Mood	2.356 (0.709-7.822)	0.161	1.004 (0.223-4.512)	0.996
Walking ability	5.540 (1.562-19.660)	**0.008***	5.250 (0.645-42.705)	0.121
Normal work	4.347 (1.315-14.369)	**0.016***	0.837 (0.089-7.810)	0.876
Enjoyment of life	7.780 (1.529-39.573)	**0.013***	14.075 (1.842-107.514)	**0.011***

**-statistically significant p value, COR-Crude Odds Ratio, AOR-Adjusted Odds ratio*

Employment status was a predictor of adequacy of pain control (*P* = 0.031). The unemployed participants were 0.085 times less likely to have adequate pain control compared to the employed participants (COR = 0.085, 95% CI = 0.009 - 0.796; *P* value = 0.031). Walking ability was significantly associated with adequacy of pain control (*P* = 0.008). Participants who reported no interference with their ability to walk were 5.540 times more likely to have adequate pain control. This was a strong association (COR = 5.540, 95% CI = 1.562 - 19.660; *P* value = 0.008). There was a significant relationship between normal working and pain control (*P* = 0.016). Participants who had no interference with their normal working were 4.347 times more likely to have adequate pain control

compared to those who had interference with their normal working (COR = 4.347,95% CI = 1.315 - 14.369; *P* = 0.016). Enjoyment of life was an independent predictor of adequacy of pain control (*P* = 0.013). Participants who enjoyed their lives were 7.780 times more likely to have adequate pain control compared to those who had interference with their enjoyment of life (COR = 7.780,95% CI = 1.529- 39.573;*P* value = 0.013). This association became stronger after multivariate analysis (*P* = 0.011).

4.12 Bivariate analysis between adherence to drugs and other variables

4.12.1 Social demographic characteristics

The association between adherence and sociodemographic characteristics was determined using Fischer's exact test and the results are shown in **table 17.** There was a statistically significant association between participants who admitted to participating in regular exercises and the level of adherence to medications (*P* = 0.008). Twenty nine (33.3%) participants who were involved in regular exercises had a high level of adherence as compared to three (10.7%) participants who did not have a regular exercise pattern. Sex was not found to be significantly associated with the level of adherence (*P* = 0.438). Similarly, there wasn't a significant relationship between age and the level of adherence (*P* = 0.282). However the younger participants (18 -35 years) were more likely to have a high level of adherence (n = 13, 44.8%) compared to the other age groups. BMI and marital status were not significantly associated with the level of adherence. Employment (*P* = 0.412) and

Table 17: Association between social demographic characteristics and adherence

Variable	Level of adherence			*P* value
Socio demographic characteristics	**Low n (%)**	**Medium (%)**	**High n (%)**	
Sex				0.438
Male	9 (75)	0 (0)	3 (25)	
Female	61 (59.2)	13 (12.6)	29 (28.2)	
Age (years)				
18 -35	14 (48.3)	2 (6.9)	13 (44.8)	0.282
36 - 55	31 (70.5)	5 (11.4)	8 (18.2)	
56 -64	13 (65)	2 (10)	5 (25)	
65 years and above	12 (54.5)	4 (18.2)	6 (27.3)	
BMI				
Below 18.5	1 (20)	1 (20)	3 (60)	0.182
18.5 – 25	27 (62.8)	2 (4.7)	14 (32.6)	
25.5 – 30	32 (62.7)	7 (13.7)	12 (23.5)	
Above 30	10 (62.5)	3 (18.8)	3 (18.8)	
Marital status				
Single	26 (59.1)	5 (11.4)	13 (29.5)	0.959
Married	44 (62)	8 (11.3)	19 (26.7)	
Employment status				
Unemployed	48 (57.8)	9 (10.8)	26 (31.3)	0.412
Employed	22 (68.8)	4 (12.5)	6 (18.8)	
Education status				
None	2 (33.3)	2 (33.3)	2 (33.3)	0.504
Primary	21 (67.7)	2 (6.5)	8 (25.8)	
Secondary	31 (63.3)	6 (12.2)	12 (24.5)	
Tertiary	16 (55.2)	3 (10.3)	10 (34.5)	
Alcohol intake				
Yes (n = 5)	5 (100)	0 (0)	0 (0)	0.382
Smoking				
Yes (n = 3	2 (66.7)	0 (0)	1 (33.3)	1.000
Regular exercises				
Yes (n = 87)	46 (52.9)	12 (13.8)	29 (33.3)	**0.008***

*- *statistically significant p value*

education status (P = 0.504) of the participants too were not significantly related to the level of adherence.

4.12.2 Classes of drugs prescribed

The association between classes of drugs and adherence was determined using Fischer's exact test and the results are shown in **table 18.** There was no significant association between any

Table 18: Association between the classes of drugs prescribed and the level of adherence

Variable	Level of adherence			*P* value
	Low n (%)	Medium n (%)	High n (%)	
DMARDS (n = 111)	67 (60.4)	13 (11.7)	31 (27.9)	1.000
Immunosuppressants (n = 5)	2 (40)	0 (0)	3 (60)	0.303
Corticosteroids (n = 58)	34 (58.6)	4 (6.9)	20(34.5)	0.160
Analgesics (n = 76)	45 (59.2)	11 (14.5)	20(26.3)	0.350
Calcium supplements(n = 47)	25 (53.2)	7 (14.9)	15 (31.9)	0.334
PPIs(n = 61)	37 (60.7)	5 (8.2)	19 (31.1)	0.478
Folic acid(n = 66)	46 (69.7)	7 (10.6)	13 (19.7)	0.057
Chondroprotective meds (n = 6)	5 (83.3)	0 (0)	1 (16.7)	0.838

of the classes of drugs used to manage RA and the level of adherence though most classes recorded more than 50% of low level of adherence. All the classes registered *P* values of more than 0.05. No specific drug had a significant association with the level of adherence ($P > 0.05$) too. Nevertheless, participants were more likely to adhere to immunosuppressants. This is because, of all the participants on immunosuppressants, 60% recorded a high level of adherence.

4.12.3 Adverse drug reactions

The association between adverse drug reactions and adherence was determined using Fischer's exact test and the results are shown in **table 19**. The occurrence of adverse drug reactions and the level of adherence to medications had no significant relationship in this study ($P > 0.05$)**.** However, all participants (100%) who reported having epigastric pain, increased blood pressure, delayed wound healing, stomatitis, respiratory infections, photosensitivity and hair loss consequently recorded a low level of adherence to medications.

Table 19: Association between adverse drug reactions and the level of adherence

Variable	Level of adherence			*P* value
	Low n (%)	**Medium n (%)**	**High n (%)**	
Nausea (n = 10)	8 (80)	1 (10)	1 (10)	0.370
Vomiting (n = 5)	3 (60)	1 (20)	1 (20)	0.632
Pruritus (n = 7)	4 (57.1)	0 (0)	3 (42.9)	0.613
Anorexia (n = 3)	1 (33.3)	1 (33.3)	1 (33.3)	0.198
Weight loss (n = 2)	0 (0)	1 (50)	1 (50)	0.075
Abdominal pain (n = 16)	13 (81.3)	1 (6.3)	2 (12.5)	0.209
Fatigue (n = 11)	7 (63.6)	1 (9.1)	3 (27.3)	1.000
Urticaria (n = 2)	0 (0)	0 (0)	2 (100)	0.151
Fever (n = 3)	2 (66.7)	0 (0)	1 (33.3)	1.000
Rash, black spots (n = 7)	3 (42.9)	1 (14.3)	3 (42.9)	0.414
Respiratory infections (n=4)	4 (100)	0 (0)	0 (0)	0.428
Stomatitis (n = 1)	1 (100)	0 (0)	0 (0)	1.000
Mucositis (n = 5)	3 (60)	1 (20)	1 (20)	0.632
Headache (n = 14)	9 (64.3)	0 (0)	5 (35.7)	0.376
Female reproductive disorder n = 1)	1 (100)	0 (0)	0 (0)	1.000
Night sweats(n = 2)	0 (0)	1 (50)	1 (50)	0.075
Cough(n = 7)	5 (71.4)	0 (0)	2 (28.6)	1.000
Back pain (n = 7)	6 (85.7)	0 (0)	1 (14.3)	0.509
Chills (n = 1)	1 (100)	0 (0)	0 (0)	1.000
Dizziness (n = 4)	1 (25)	0 (0)	3 (75)	0.127
Delayed wound healing(n = 1)	1 (100)	0 (0)	0 (0)	1.000
Diabetes mellitus(n = 1)	0 (0)	1 (100)	0 (0)	0.113
Insomnia (n = 6)	3 (50)	2 (33.3)	1 (16.7)	0.232
Increased blood pressure (n = 3)	3 (100)	0 (0)	0 (0)	0.687
Epigastric pain (n = 2)	2 (100)	0 (0)	0 (0)	1.000
Constipation (n = 2)	0 (0)	0 (0)	2 (100)	0.151
Corneal changes (n = 5)	3 (60)	0 (0)	2 (40)	0.809

4.12.4 Social and economic factors

The association between socioeconomic factors and adherence was determined using Fischer's exact test and the results are shown in **table 20.** For all the patients who had socioeconomic issues, sixty one (74.4%) had a low level of adherence. The statistically significant issues were lack of finances ($P < 0.001$) and inadequate knowledge about their treatment ($P = 0.007$). All the thirteen (100%) participants who revealed they had inadequate knowledge about their treatment had a low level of adherence. The association

between culture and beliefs about illness and the level of adherence was not significant (*P* = 0.183).

Table 20: Association between social and economic factors and the level of adherence

Variable	Level of adherence			*P* value
	Low n (%)	**Medium n (%)**	**High n (%)**	
Lack of finances (n = 81)	60 (74.1)	8 (9.9)	13 (16)	**< 0.001***
Culture and beliefs about illness(n = 6)	6 (100)	0 (0)	0 (0)	0.183
Inadequate knowledge of treatment(n = 13)	13 (100)	0 (0)	0 (0)	**0.007***

**-statistically significant p value*

4.12.5 Therapy related factors

The association between therapy related factors and adherence was determined using Fischer's exact test and the results are shown in **table 21**. Condition related factors were significantly associated with the level of adherence (*P* < 0.001) whereby fifty four (88.5%) participants had a low level of adherence. The level of disability significantly affected the adherence levels (*P* < 0.001) where twenty (95.2%) participants who reported some level of disability recorded low adherence levels. There was also a significant association between severity of disease and the level of adherence (*P* < 0.001). Patients who mentioned the duration of treatment (*P* < 0.001) was long recorded a low level of adherence to medication. Complexity of the medical regimen was significantly associated with the level of adherence (*P* = 0.016) as participants who said their regimens were complex had a low level of adherence (n = 13, 83.3%). Presence of an adverse drug reaction as a patient related factor was significantly associated with the level of adherence (*P* < 0.001). Of the forty one patients who reported an adverse drug reaction affected their adherence to medications, thirty eight (83.3%) had low adherence levels.

Table 21: Association between therapy related factors and the level of adherence

Variable	Level of adherence			*P* value
	Low n (%)	**Medium n (%)**	**High n (%)**	
Level of disability(n = 21)	20 (95.2)	0 (0)	1 (4.8)	**0.001***
Severity of the disease (n = 59)	53 (89.8)	3 (5.1)	3 (5.1)	**< 0.001***
Duration of treatment(n = 54)	50 (92.6)	2 (3.7)	2 (3.7)	**< 0.001***
Complexity of the medical regimen(n = 15)	13 (86.7)	2 (13.3)	0 (0)	**0.016***
Frequent changes in treatment(n = 6)	5 (83.3)	1 (16.7)	0 (0)	0.345
Adverse drug reactions(n = 41)	38 (92.7)	1 (2.4)	2 (4.9)	**< 0.001***
Patient related factors(n = 68)	57 (83.8)	6 (8.8)	5 (7.4)	**< 0.001***
Did not know I had to take drugs daily(n = 43)	39 (90.7)	3 (7)	1 (2.3)	**< 0.001***
Forgetfulness (n = 60)	54 (90)	4 (6.7)	2 (3.3)	**< 0.001***
Anxiety of possible adverse effects(n = 43)	38 (88.4)	1 (2.3)	4 (9.3)	**< 0.001***
Misunderstanding of treatment instructions(n = 18)	17 (94.4)	1 (5.6)	0 (0)	**0.002***
Fear of dependence (n = 8)	8 (100)	0 (0)	0 (0)	0.091

**-statistically significant p value*

Patient related factors including forgetfulness, anxiety of possible side effects and not knowing if they had to take drugs daily were significantly associated with the level of adherence each recording a *P* value of less than 0.001. Misunderstanding of treatment instructions was also significant (*P* = 0.002). Seventeen (94.4%) participants who misunderstood their treatment instructions had low levels of adherence.

4.12.6 Hospital related factors

The association between hospital related factors and adherence was determined using Fischer's exact test and the results are shown in **table 22.** Hospital related factors played a

Table 22: Association between hospital related factors and the level of adherence

Variable	Level of adherence			*P* value
	Low n (%)	**Medium n (%)**	**High n (%)**	
Hospital related factors(n = 51)	43 (84.3)	3 (5.9)	5 (9.8)4	< **0.001***
Drug unavailable in pharmacy(n = 28)	25 (89.3)	1 (3.6)	2 (7.1)	**0.002***
Drug is unaffordable(n = 50)	43 (86)	3 (6)	4 (8)	< **0.001***
Concerns not addressed(n = 4)	4 (100)	0 (0)	0 (0)	0.428
Instructions not clear(n = 15)	14 (93.3)	1 (6.7)	0 (0)	**0.008***

**-statistically significant p value*

significant role in determining the level of adherence ($P < 0.001$) whereby the unavailability of drugs in the hospital pharmacy significantly affected the level of adherence ($P = 0.002$) in that, twenty five (89.3%) participants who missed their drugs in the hospital pharmacy recorded a low level of adherence. Drug unaffordability was also significant ($P < 0.001$). Many patients (n = 43, 86%) missed drugs because they could not afford them.

4.12.7 Adequacy of pain control

The association between the level of pain control and adherence was determined using Fischer's exact test and the results are shown in **table 23**. Presence of pain on the day of the interview was significantly associated with the level of adherence ($P = 0.002$). Sixty three (67.7%) participants who reported feeling pain had low levels of adherence as opposed to thirteen (59.1%) participants who reported no pain and had a high level of adherence. There was no significant association between the level of pain and the level of adherence ($P = 0.180$). There was a significant relationship between the amount of relief from pain medications and the level of adherence ($P = 0.053$). All the patients who reported

50% relief from pain medications had a low level of adherence while half of the patients who reported 100% relief from pain medication had a high level of adherence.

Table 23: Association between pain control and the level of adherence

Variable	**Level of adherence**			***P* value**
	Low n (%)	**Medium n (%)**	**High n (%)**	
Joint pain (n = 93)	63 (67.7)	11 (11.8)	19 (20.4)	**0.002***
Level of pain (n=93)				0.180
Mild (n = 26)	16 (61.5)	2 (7.7)	8 (30.8)	
Moderate (n = 19)	11 (57.9)	5 (26.3)	3 (15.8)	
Severe (n = 48)	36 (75)	4 (8.3)	8 (16.7)	
Pain on average				0.339
No pain (n = 5)	2 (40)	0 (0)	3 (60)	
Mild (n = 38)	19 (50)	6 (15.8)	13 (34.2)	
Moderate (n = 21)	14 (66.7)	3 (14.3)	4 (19)	
Severe (n = 51)	35 (68.6)	4 (7.8)	12 (23.5)	
Relief from pain medication				**0.053***
30% (n = 2)	1 (50)	0 (0)	1 (50)	
40% (n = 3)	1 (33.3)	0 (0)	2 (66.7)	
50% (n = 5)	5 (100)	0 (0)	0 (0)	
60% (n = 16)	14 (87.5)	0 (0)	2 (12.5)	
70% (n = 30)	18 (60)	5 (16.7)	7 (23.3)	
80% (n = 35)	22 (62.9)	6 (17.1)	7 (20)	
90% (n = 18)	6 (33.3)	2 (11.1)	10 (55.6)	
100% (n = 6)	3 (50)	0 (0)	3 (50)	

**-statistically significant p value*

4.12.8 Pain interference with activities of daily living

The association between pain interference with activities of daily living and adherence was determined using Fischer's exact test and the results are shown in **table 24**. The mood was significantly associated with the level of adherence ($P < 0.001$). Patients (n = 16, 50%) who cited no interference had high levels of adherence to medications while patients who claimed high levels of interference with their moods (n = 34, 72.3%) recorded low levels of adherence. Pain interference with the walking ability was not significantly associated with the level of adherence ($P = 0.510$). The effect of pain on the interference with interpersonal relations was significantly associated with the level of adherence ($P = 0.006$). Of the Participants who said pain did not interfere with their relations, sixteen (48.5%) had a high level of adherence while among those participants who said pain really interfered with their relations, twenty five (80.6%) recorded low levels of adherence. Enjoyment of life and the level of adherence were significantly related ($P = 0.017$). Eight (50%) of the participants who cited no interference with their enjoyment of life had high level of adherence while thirty six (76.6%) of those who stated a high interference with their enjoyment of life had low levels of adherence.

Table 24: Association between the level of interference with daily activities and the level of adherence

Variable	Level of adherence			*P* value
	Low n (%)	Medium n (%)	High n (%)	
Mood				**0.001***
No interference	10 (31.3)	6 (18.8)	16 (50)	
Low interference	26 (72.2)	5 (13.9)	5 (13.9)	
High interference	34 (72.3)	2 (4.3)	11 (23.4)	
Walking ability				0.510
No interference	3 (42.9)	1 (14.3)	3 (42.9)	
Low interference	18 (62.1)	2 (6.9)	9 (31)	
High interference	49 (62)	10 (12.7)	20 (25.3)	
Normal work				0.323
No interference	3 (50)	0 (0)	3 (50)	
Low interference	12 (50)	5 (20.8)	7 (29.2)	
High interference	55 (64.7)	8 (9.4)	22 (25.9)	
Relations with other people				**0.006***
No interference	13 (39.4)	4 (12.1)	16 (48.5)	
Low interference	32 (62.7)	8 (15.7)	11 (21.6)	
High interference	25 (80.6)	1 (3.2)	5 (16.1)	
Sleep				0.118
No interference	6 (37.5)	2 (12.5)	8 (50)	
Low interference	21 (56.8)	4 (10.8)	12 (32.4)	
High interference	43 (69.4)	7 (11.3)	12 (19.4)	
Enjoyment of life				**0.017***
No interference	6 (37.5)	2 (12.5)	8 (50)	
Low interference	28 (53.8)	9 (17.3)	15 (28.8)	
High interference	36 (76.6)	2 (4.3)	9 (19.1)	

**- statistically significant p value*

4.12.9 Logistic regression analysis of predictors of the level of adherence to medications

Logistic regression analysis was employed to determine the predictors of adherence to medicines and the results are shown in **table 25**. The level of adherence was the dependent variable which was a binary outcome. Adherence and no adherence were assigned 1 and 0 values respectively. Regular exercises was an independent predictor of the level of adherence (P = 0.029) on bivariate analysis and multivariate analysis (P = 0.032) respectively. Participants who performed regular exercises were 4.167 times more likely to have a high

Table 25: Predictors of the level of adherence

Variable	Bivariate analysis	*P* value	Multivariate analysis	*P* value
	COR (95% CI)		AOR (95% CI)	
Age	0.985 (0.960 - 1.010)	0.251	0.987 (0.956 - 1.017)	0.388
Employment status	0.506 (0.185 - 1.377)	0.182	0.370 (0.126 - 1.083)	0.070
Regular exercises	4.167 (1.161 - 14.953)	**0.029***	4.235 (1.131 - 15.849)	**0.032***
DMARDs	1.162 (0.116 - 11.604)	0.898	5.811 (0.248 -135.897)	0.274
Corticosteroids	1.973 (0.856 - 4.552)	0.111	1.581 (0.654 - 3.821)	0.308
Analgesics	0.803 (0.343 - 1.881)	0.614	0.683 (0.273 - 1.706)	0.415
Folic acid	0.387 (0.167 - 0.893)	**0.026***	0.348 (0.144 - 0.847)	**0.020***
Abdominal pain	0.329 (0.070 - 1.536)	0.157`	0.095 (0.005 - 1.670)	0.108
Lack of finances	0.150 (0.061 - 0.371)	**< 0.001***	0.651 (0.182 - 2.334)	0.510
Level of disability	0.101 (0.013 - 0.792)	**0.029***	1.677 (0.097 - 28.965)	0.722
Severity of the disease	0.049 (0.013-0.178)	**< 0.001***	0.171 (0.029 - 1.011)	**0.052***
Duration of treatment	0.397 (0.008 - 0.177)	**< 0.001***	0.464 (0.059 - 3.655)	0.467
Adverse drug reactions	0.075 (0.016 - 0.335)	**0.001***	0.159 (0.008 - 2.878)	0.214
Non-compliant	0.031 (0.004 - 0.242)	**0.001***	0.206 (0.013 - 3.096)	0.254
Forgetfulness	0.028 (0.006 - 0.129)	**< 0.001***	0.196 (0.026 - 1.452)	0.111
Anxiety of ADRs	0.161 (0.051 - 0.500)	**0.002***	3.560 (0.255 - 49.542)	0.344
Drug unavailable in pharmacy	0.146 (0.032 - 0.658)	**0.012***	2.883 (0.293 - 28.292)	0.363
Drug is unaffordable	0.114 (0.037 - 0.356)	**< 0.001***	0.163 (0.027 - 0.971)	**0.046***
Relief from medications	1.025 (0.994 - 1.058)	0.109	1.000 (0.957 - 1.044)	0.997
Mood	0.549 (0.329 - 0.917)	**0.022***	2.066 (0.618 - 6.907)	0.238
Relations with other people	0.419 (0.229 - 0.766)	**0.005***	0.232 (0.072 - 0.749)	**0.015***
Sleep	0.491 (0.280 - 0.861)	**0.013***	1.084 (0.408 - 2.879)	0.870
Enjoyment of life	0.500 (0.273 - 0.913)	**0.024***	0.770 (0.224 - 2.638)	0.677

**-statistically significant p value, COR-Crude Odds Ratio, AOR-Adjusted Odds ratio*

level of adherence to medications compared to participants who shied from participating in regular exercises (COR = 4.167,95% CI = 1.161 - 14.953; *P* value = 0.029). Folic acid was significantly associated with the level of adherence (*P* = 0.026).The association became stronger on multivariate analysis *(P* = 0.020). Participants who were prescribed for folic acid were 0.387 times less likely to have a high level of adherence (COR = 0.387, 95% CI = 0.167 - 0.893; *P* value = 0.026). Lack of finances was a predictor of the level of adherence (*P* < 0.001). Participants who revealed that lack of finances affected their level

of adherence to medications were 0.150 times likely to have a high level of adherence (COR = 0.150, 95% CI = 0.061 - 0.371; *P* value < 0.001). The level of disability was significantly associated with the level of adherence (*P* = 0.029). Participants who didn't report any disability were 0.101 times less likely to have a low level adherence. Participants who didn't report any disability were 0.101 times likely to have a low level of adherence (COR = 0.101, 95% CI = 0.013 - 0.792; *P* value = 0.029). Severity of the disease was an independent predictor of the level of adherence (*P* < 0.001) on bivariate analysis and *P* = 0.052 on multivariate analysis). Patients who stated that severity of the disease affected their level of adherence were 0.049 times likely to have a high level of adherence (COR = 0.049, 95% CI = 0.013 - 0.178; *P* value < 0.001). The unaffordability of drugs was an independent predictor of the level of adherence (*P* < 0.001 on bivariate analysis and *P* = 0.046 on multivariate analysis). Participants who said unaffordability of drugs affected their level of adherence were 0.114 times likely to have a high level of adherence (COR = O.114, 95% CI = 0.037 - 0.356; *P* < 0.001).

Relations with other people was an independent predictor of the level of adherence (*P* = 0.005 on bivariate and *P* = 0.015 on multivariate analysis) (COR = 0.419, 95% CI = 0.229 - 0.766; *P* = 0.005). Participants who had no interference with their relations with other people were 0.419 times likely to have low levels of adherence. Other factors that were significantly associated with the level of adherence posting *p* values that were less than 0.024 included duration of treatment, occurrence of adverse drug reactions, non-compliance, forgetfulness, anxiety of possible adverse effects, unavailability of drugs in the hospital pharmacy, mood, sleep and enjoyment of life. Participants who were anxious about developing an adverse effect were 0.161 times likely to have a high level of adherence (COR = 0.161, 95% CI = 0.051 - 0.500; *P* = 0.002).

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Introduction

The study findings were discussed within the perspective of the previous literature. The research findings guided the conclusion and the recommendations.

5.2 Discussion

There was a female predominance in this study. This tallies with several other studies that report a female preponderance in most rheumatological diseases both in urban and rural areas (38). A similar study reported an increased frequency of rheumatoid arthritis in females compared to males recording an incidence rate of four to five times higher below the age of 50 years old (39) (40). This could be attributed to the variable actions of the male and female hormones on the immune system where the male hormones appear to suppress it while the female hormones stimulate it. The natural rise and fall of the female hormones in the body could be a factor too especially during menstruation, pregnancy,menopause and hormonal replacement therapy. The female health seeking behavior could also be a factor. The mean age was 48 years old. This coincides with a study done in the same setting that reported a female dominated participation and a mean age of 41 years old (41). Another study reported that rheumatoid arthritis can start at any age but peaks between 40 and 60 years or older for men citing that prevalence increased with age (6). Alcohol intake and smoking recorded the lowest participation in the study. This was consistent with another study that reported alcohol intake and smoking were lower in patients with rheumatoid arthritis than the non rheumatoid arthritis ones (40). This could be attributed to the female predominance aspect of this disease since they practice these habits less than male.

Almost all participants had a formal education with those who attended secondary school recording the highest participation. Another study reported similar findings (40). This could be explained by the fact that the study was done in an urban setting. Majority of the participants engaged in various aspects of regular exercises. This was contrary to another study that reported 71% of patients with rheumatoid arthritis did not participate in any form of regular exercise (42). However, there were similar barriers to exercise among patients

who exercised and those who didn't. They included fatigue and pain. Those who engaged in exercises were able to overcome them.

DMARDs were the treatment of choice and the most prescribed. This finding was consistent with another one where 82.1% of patients were using them (16). DMARDs were preferred because they modify the immune system to slow the disease progression by reducing joint inflammation that causes pain and joint destruction (43). Methotrexate was the recommended first line for active rheumatoid arthritis unless contraindicated. This was in agreement with another study that reported 75% of the patients being on methotrexate (44). Methotrexate was the preferred first line because it was more of an anti inflammatory agent than an immunosuppressant in RA. Its inhibition of interleukin 1 and other inflammatory cytokines brought about a rapid clinical response after its initiation (45). Methotrexate works better than any other single DMARD. Its quite affordable, generally safer for long periods and suitable for children too (43) (46). Most patients in this study were on two or more DMARDs. This was consistent with another study that found combination therapy with more than one DMARD was more effective though with the risk of more adverse effects. Leflunomide may be an alternative to methotrexate or given in combination. Sulfasalazine and hydroxychloroquine are preffered for low disease activity (17). Corticosteroids have potent anti inflammatory effects and therfore are effective adjuvants in rheumatoid arthritis. Long term adverse effects and toxicity have reduced the clinical benefit of these drugs for continued use. Corticosteroids are therefore used for short term management of inflammation in patients with recent onset of rheumatoid arthritis and disease flares (14). Fifty percent of prescriptions in this study had a corticosteroid prescribed. Another study had 72% of the patients on a corticosteroid (44). NSAIDs were prescribed for 66.1% of the participants. These agents have anti inflammatory, antipyretic and analgesic properties and are thus used to control pain. NSAIDs are often used without considering their relative contraindications. Its thus recommended that they are used at their lowest effective dose for the shortest duration of time (14). Fifty three percent of prescriptions had a proton pump inhibitor. This was consistent with other studies that suggested a PPI should be co prescribed with NSAIDs to reduce the gastro intestinal side effects that include gastric erosions, peptic ulcers, dyspepsia, flatulence,nausea, vomiting, gastroesophageal reflux, bleeding,perforation and gastric outlet obstruction (18) (47).

Comorbidities were reported in fifty one (44.4%) participants. This figure closely tallies with another study that observed 44.9% comorbidities among patients with rheumatoid arthritis (44). Hypertension was the most reported cormobidity. It also featured prominently in other reported cormobidities among other studies. An increase in comorbidity could also enhance the disease severity. Some studies found an increased rate of co existing diseases in patients with rheumatoid arthritis compared to the general population. The presence of rheumatoid arthritis is a significant predictor of an increase in cormobidity (48). Cormobidities and extra articular manifestations are markers of severity of the disease. Presence of pericarditis,vasculitis,pleuritic or felty's syndrome are correlated with a poor prognosis (49).

Abdominal pain and headache were the most prevalent adverse drug effects. Epigastric pain was reported by few participants probably due to the co prescription of a proton pump inhibitor that helped reduce the occurences of gastro intestinal adverse effects. Increase in blood pressure was revealed by 2.6% of the participants probably on NSAIDs. A previous study reported that most drugs used in management of rheumatoid arthritis have a possibility of causing an adverse drug reaction or putting the body in a vulnerable state. The key drugs have an immunosuppressant component. They predispose the patient to increased risk of infections, gastrointestinal irritability exhibiting symptoms such as nausea, vomiting and diarrhea. Methotrexate can further cause abnormal liver function, mouth sores, hair loss and chronic cough (20). Sulfasalazine increases sun sensitivity. NSAIDs cause gastrointestinal side effects and increased cardiovascular risks. They may also increase blood pressure in hypertensive patients (15).

Majority of the participants were non adherent to drugs. The reasons for non adherence were socioeconomic factors, patient related factors, hospital related factors, therapy related factors and condition related factors. All the factors significantly related to the level of adherence. Adherence to chronic therapy is often sub optimal and adherence is a critical component in evaluation of the effectiveness of a given therapy. Non adherence contributes to treatment failure, delayed recovery and progression of disease (16). Previous researches have reported that patients with rheumatoid arthritis prefer taking the drugs in lower doses and less frequently than recommended. Many patients with RA do not take their

medications before an activity and that they are reluctant to take their pain medications unless unable to tolerate the pain (27). These patients preferred complementary therapy as opposed to conventional treatments. They cited lower incidences of adverse drug reactions, psychological comfort, greater patient choice and an increased quality of patient therapist relationship (28). Other RA studies demonstrated overall inadequate treatment adherence (50) (51).

Most participants reported pain of varying degrees and their daily activities were interfered with at various levels. This was consistent with another study that showed forty seven percent of patients reported that the worst impact of arthritis was on their capacity to work (52).

On bivariate analysis, the employment status was found to be significantly associated with pain control. Most of the employed participants reported no pain compared to the unemployed ones who had severe pain. This was consistent with other studies. A study done in England showed that half of the patients with RA were in paid employment at onset but work disability became an adverse outcome for a third of them by five years (53). This clearly depicted that remaining in employement was a factor of how adequately the disease(pain) was controlled. Immunosuppressants were found to be significantly associated with adequacy of pain control. No patient on an immunosuppressant reported severe pain. This was more evident with patients who started the treatment early. Early treatment reduces disease progression, rate of joint damage and minimize pain (54) (55).

There was a significant association between fatigue and adequacy of pain control. Patients who felt fatigued after medications experienced severe pain. The occurrence of an adverse drug reaction was significantly associated with adequacy of pain control. A study done in Colombia reported that 73.2% of patients who experienced an adverse drug reaction stopped taking their medicines though the ADRs reported were mostly among patients on biological DMARDs (56). A systematic review on the safety of non steroidal anti-inflammatory drugs (celecoxib and Etoricoxib) revealed mild adverse events such as nausea, vomiting and headache (57).

There was a significant relationship between pain control and the participants' moods. There was also a significant relationship between pain control and normal work, sleep and

enjoyment of life . A study in Australia concluded that persons with arthritis demonstrate marked pain related functional impairment characterized by difficulty with many aspects of daily living (52).

There was a statistically significant association between participants who admitted to participating in regular exercises and the level of adherence to medications. This could be attributed to the patients' discipline and attitude towards their treatment. Patients with RA who exercise may experience less pain compared to those who don't. Exercises reduce painful symptoms, improve joint function and flexibility, increase range of motion and boost the mood (58). There wasn't a significant association between any of the classes of drugs used to manage RA and the level of adherence though most classes recorded more than 50% of low level of adherence. All the classes registered *P* values that were more than 0.05. Lack of finances and inadequate knowledge about their treatment stood out as the social economic factors that significantly related to the level of adherence to medications. This could be explained by the high unemployment levels among these patients and limited health literacy concerning their disease and treatment (59). The level of disability significantly affected the adherence levels. Long duration of treatment was significantly associated with the level ofadherence. There was also a significant association between the complexity of the medical regimen and the level of adherence as participants who said their regimens were complex had a low level of adherence. This could be explained by the patients' limited knowledge on their disease status. Presence of an adverse drug reaction as a patient related factor was significantly associated with the level of adherence.

Patient related factors including forgetfulness, anxiety of possible side effects and not knowing if they had to take drugs daily were significantly associated with the decreased level of adherence. Misunderstanding of treatment instructions was also significant. The unavailability of drugs in the hospital pharmacy significantly affected the level of adherence. There was a significant relationship between the amount of relief from pain medications and the level of adherence. The above findings are consistent with another study that agreed to the fact that medication non adherence is a common problem among RA patients and that non adherence is a dynamic, multifaceted issue affected by patient factors, disease factors and characteristics (59). Pain interference with the participants'

moods was significantly associated with the level of adherence. Patients who cited no interference had high levels of adherence to medications while patients who claimed high levels of interference with their moods recorded low levels of adherence. The mood of these patients is usually affected by the social context of the individual and the biologic disease state. This concurs with another study that points out that mood disturbances and depressive tendencies are common among patients with rheumatoid arthritis (60).

5.3 Study strengths and weaknesses

The participants and the research assistants were very cooperative and thus made it possible for the study to be completed within the stipulated time. However , the study was prone to information bias since it majorly depended on the participants account of events.

5.4 Conclusion

Rheumatoid arthritis was more prevalent in females at Kenyatta National Hospital. The conventional DMARDs were the most prescribed class of drugs. Corticosteroids, analgesics, proton pump inhibitors and folic acid were co prescribed where necessary. The prevalence of reported adverse drug reactions was low with abdominal pain and headache being the most reported adverse effects. However , the occurrence of an adverse drug reaction or anxiety of a possible adverse effect significantly related to the adequacy of pain control. Low levels of medication adherence significantly affected the adequacy of pain control and therefore pain was generally inadequately controlled. Optimal care of patients with rheumatoid arthritis needs an intergrated approach that includes both pharmacologic and non pharmacologic therapies.

5.5 Recommendations

5.5.1 Recommendations for policy and practice

1. Patient education on the disease should be enhanced. This is because many patients hoped to stop taking their medicines after getting cured. And many were worried about the duration of treatment.
2. Patient literacy on the type of drugs used to manage rheumatoid arthritis and why the DMARDs should be initiated as soon as a diagnosis is made. This is because many patients preferred the analgesics to DMARDs due to cost implications. They are not aware that the analgesics will not slow the disease progression and joint damage.

3. Patient knowledge about the expected adverse effects putting emphasis on what should be done in case of an occurrence should be enhanced. Many patients prefer stopping a drug and not reporting the incident unless probed.
4. Intensive adherence counselling should be done to the patients. Clinicians should find out the reasons for non adherence during the patient education sessions and address them at personal level.

5.5.2 Recommendation for research

A study should be done to assess the impact of patient health literacy on management of rheumatoid arthritis.

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APPENDICES

APPENDIX 1: SCREENING AND ELIGIBILITY FORM

All subjects enrolled must meet eligibility criteria based on the inclusion/exclusion criteria detailed in the application approved by the KNH/UoN Research and Ethics Committee.

I. Study information

Study title: Evaluation of pain management among patients with rheumatoid arthritis at Kenyatta National Hospital.

Principal investigator: Laurine Muyuka Mukopi

Signature ……

Date of screening…….

II. Patient information

Patient code ……

Gender: Male ☐ Female ☐

III. Inclusion/ exclusion criteria (Tick where appropriate)

Inclusion criteria		
Items 1 – 6 need to be answered YES for eligibility	**YES**	**NO**
Aged 18 years and above		
Clinical diagnosis of Rheumatoid arthritis		
Rheumataoid arthritis patient on treatment		
Voluntary informed consent given		
Proxy consent given (where applicable)		
Patient attending clinic at KNH		
Exclusion criteria (items 1-3) need to be answered YES		
Declined to give informed consent		
Rheumatoid Arthritis patient not on treatment		
Rheumatoid arthritis patient with mental instability or cognitive impairment		

APPENDIX 2A: CONSENT EXPLANATION FORM

Patient ☐

Caregiver ☐ Relation to the patient……

Study title: Evaluation of pain management among patients with rheumatoid arthritis at Kenyatta National Hospital.

Institution: Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi, P.O BOX 30197 – 00400, Nairobi.

Principal investigator: Dr. Laurine Muyuka Mukopi, post graduate student (clinical pharmacy) P.0 BOX 64 – 50136, MATETE.

Supervisors: Dr. Peter Karimi, PhD, Lecturer, Department of pharmaceutics and Pharmacy Practice, University of Nairobi.

Dr. Samuel C. Gitau, PhD, Department of pharmacy/ Alternative Medicine, Kenyatta University.

I am Dr. Laurine Muyuka Mukopi conducting the above study to partly fulfill the requirements for a Master's degree in clinical Pharmacy of the University of Nairobi.

Ethical approval

Kenyatta National Hospital/University of Nairobi Ethical and Research Committee.

What is the purpose of the study?

The study you are being requested to participate in aims at evaluating the various pain management practices, any adverse drug reactions experienced and their relation to the level of pain control among patients with rheumatoid arthritis.

Why have I been invited to participate?

You have been approached for consideration as a participant because you are an adult patient aged 18 years and above with rheumatoid arthritis attending clinic at Kenyatta National Hospital.

What is expected of me as a participant?

Should you agree to participate in the study, you will be asked to be interviewed using a structured questionnaire to collect socio demographic data and medical history. This will take less than an hour of you time.

Who will have access to the collected data?

All data collected from you will be coded and entered into a password protected computer without access to the public in order to protect your identity. Only the research investigator will have access to the personal information. However, ethics review committee members may access the information if need be to inspect research records. At the end of the study, there will be no way to link your name with the collected data. Any published work arising from the study will not bear your name or any other direct identifier.

Must I participate?

Your participation is completely voluntary. If you decide to participate you are free to withdraw or refuse to answer any questions at any time without jeopardizing your treatment at KNH. You will not be required to give any reason for such withdrawal or refusal.

Are there any benefits of participating?

The findings obtained from this study will be used to improve rheumatic pain management practices and hence improve the quality of your life. They'll also be used to develop future policies regarding pain management among patients with rheumatoid arthritis and identify gaps for further research and innovative strategies in pain management.

What are the risks associated with my participation?

No risk or harm is anticipated in this study. However it is possible that you might not be comfortable answering some of the questions in the study tools. All information obtained will be treated in confidence.

What will happen to the study findings?

The study findings will form part of the master's degree in clinical pharmacy project dissertation. This will further be published in a peer reviewed journal. The findings will also be shared with the University of Nairobi College of health sciences administration, Kenyatta National Hospital administration and in presentations at scientific conferences.

What do I do in case of a problem?

You are free to raise any concerns about your rights as a participant in this study to me or KNH-UoN ethics and research committee who have approved this study.

If patient only understands Kiswahili use the section below

Mgonjwa ☐

Mlezi ☐ Uhusiano na Mgonjwa……

Kuhusu utafiti huu: Tathmini ya jinsi uchungu unavyoshughulikiwa kati ya wagonjwa wa yabisi baridi (Rheumatoid Arthritis) katika hospitali kuu ya Kenyatta.

Taasisi: Idara ya Pharmaceutics and Pharmacy practice, shule ya pharmacy, chuo kikuu cha Nairobi, S.L.P. 30197- 00400, Nairobi.

Mtafiti mkuu: Dkt. Laurine Muyuka Mukopi, mwanafunzi wa uzamili (utabibu dawa), S.L.P. 64 – 50136, MATETE.

Wasimamizi: Dkt. Peter Karimi, mhadhiri, Idara ya Pharmaceutics and Pharmacy practice, Chuo Kikuu cha Nairobi.

Dkt. Samuel C. Gitau, Idara ya Pharmacy/ Madawa mbadala, Chuo kikuu cha Kenyatta.

Mimi ni Dkt. Laurine Muyuka Mukopi ninafanya utafiti huu kutimiza sehemu ya mahitaji ya shahada ya uzamili katika utabibu dawa, chuo kikuu cha Nairobi.

Idhini ya kimaadili:

Kamati ya kimaadili na utafiti ya hospitali kuu ya Kenyatta/chuo kikuu cha Nairobi

Nini madhumuni ya utafiti?

Utafiti huu unalenga kutathmini njia mbalimbali za kushughulikia uchungu kati ya wagonjwa wa yabisi baridi, kuangazia matukio yasiyofaa ya madawa na jinsi yanavyohusiana na kiwango cha uchungu.

Mbona mimi nimeaalikwa kushiriki?

Umealikwa kuwa mshiriki kwa sababu wewe ni mtu mzima mwenye umri wa miaka kumi na minane na zaidi, una ugonjwa wa yabisi baridi na unapokea matibabu katika hospitali kuu ya Kenyatta.

Nini kinachotarajiwa kwangu kama mshiriki?

Ukikubali kuwa mshiriki utahojiwa kwa kutumia muundo wa dodoso kukusanya nakala za kijamii na historia ya matibabu yako. Hii shughuli haitachukua muda mrefu itakuwa chini ya saa moja.

Nani watakuwa na fursa ya nakala zilizokusanywa?

Nakala zozote zitakazotokana na huu utafiti zitahifadhiwa kwa siri na zitatumika tu kwa utafiti huu. Baada ya kumaliza utafiti huu hakuna jinsi jina lako litahusishwa na kiungo chochote cha utafiti huu. Kazi itakayochapishwa kutokana na utafiti huu haitakuwa na kitambulisho chako chochote.

Ni lazima ni shiriki?

Kushiriki katika utafiti huu ni hiari yako. Iwapo utakubali kushiriki bado utakuwa huru kuondoka ama kukataa kujibu swali lolote wakati wowote ule bila kuweka matibabu yako hapa KNH hatarini. Si lazima upeane sababu ya kuondoka ama kukataa kushiriki katika utafiti huu.

Kuna faida ya kushiriki?

Matokeo ya utafiti huu yatatumiwa kuboresha jinsi ya kushughulikia uchungu unaotokana na yabisi baridi na baadaye kuboresha hali ya maisha ya wagonjwa wa yabisi baridi. Matokeo haya pia yatatumiwa kutengeneza sera zitakazohusu matibabu ya uchungu, huku yakiangazia mapengo yatakayohitaji utafiti zaidi wa njia zingine mwafaka za kushughulikia uchungu.

Nini hatari za kushiriki?

Hakuna hatari inayotarajiwa katika utafiti huu. Kuna uwezekano kuwa utakosa starehe ya kujibu maswali mengine utakayoulizwa. Taarifa zote ambazo zitachukuliwa katika utafiti huu zitawekwa kisiri.

Matokeo ya utafiti yatafanyiwa nini?

Matokeo ya utafiti yatakuwa sehemu moja ya mradi wa shahada ya uzamili wa utabibu dawa. Pia yatachapishwa katika jarida la mapitio ya rika. Na yatapewa wasimamizi wa hospitali kuu ya Kenyatta, wasimamizi wa chuo kikuu cha Nairobi kitengo cha sayansi ya afya na pia kuwasilishwa katika mikutano ya kisayansi.

Nitafanya nini ikiwa kutatokea shida?

Utakuwa huru kuangazia wasiwasi wowote kama mshiriki katika utafiti huu kwangu au kwa Kamati ya kimaadili na utafiti ya KNH-UoN ambayo imeidhinisha utafiti huu.

APPENDIX 2B: CONSENT DECLARATION FORM

Informed consent

Patient ☐

Caregiver ☐ **Relation to the patient……..**

I, the undersigned, willingly agree to participate in this study. I have read and understood the nature of the study, my responsibilities as a study participant, the inconveniences associated with voluntary participation in the study and that all my questions and concerns relating to the study have been answered satisfactorily.

I understand that I may choose to leave the study at any time and will not be prejudiced or penalized in any way. I understand that the information gathered will be used for the purposes of this study only and maximum confidentiality will be maintained.

I will receive a copy of this signed consent document to take way and keep.

Respondent's name……..

Signature……..

Date……..

Witness (colleague)

Signature……..Date ……

Investigator's statement

I, the undersigned, have explained the information in this document to this participant and encouraged them to ask questions which I took time to answer. I am satisfied that the participant adequately understands all aspects of the research as discussed in the consent process information document above.

……

Name and signature of person obtaining consent.

In case of any concern you may contact the following principal investigator on email: skymuyuka@yahoo.com/ 0721948363 or KNH-UoN Ethics and Research Committee secretary: Prof Mark Chindia. Tel: + 254207726300.ext. 44355, email: uonknh.ac.ke

If patient only understands Kiswahili use the section below

RIDHAA

Mgonjwa ☐

Mlezi ☐ **Uhusiano na mgonjwa**……..

Mimi, mtiaji sahihi kwa hiari yangu nimekubali kushiriki katika utafiti huu. Nimesoma na kuelewa asili ya utafiti, majukumu yangu kama mshiriki, usumbufu unaohusiana na hiari yangu ya kushiriki katika utafiti huu na maswali pamoja na wasiwasi wangu kuhusu utafiti huu yamejibiwa kwa kuridhisha.nimeelewa kuwa naweza acha kushiriki katika utafiti huu wakati wowote bila kuweka matibabu yangu hatarini. Nimeelewa kuwa taarifa zozote kutokana na utafiti huu zitatumika kwa utafiti huu pekee na usiri utahakikishwa wakati wote. Nitapata nakala yangu ya ridhaa iliyowekwa sahihi niiweke.

Jina la anayejibu……

Sahihi……....

Tarehe…….

Shahidi (mwenzangu)

Sahihi…….Tarehe……

Kauli ya mtafiti

Mimi, mtiaji sahihi, nimeelezea taarifa iliyomo katika hati hii kwa mshiriki na nikamuhimiza kuuliza maswali ambayo nimejibu. Nimeridhika kuwa mshiriki anaelewa vizuri vipengele vinavyohusiana na utafiti kama vilivyoelezwa katika mchakato wa ridhaa uliyo hapo juu.

…….

Jina na sahihi ya mwenye kuchukua ridhaa.

Kwa maelezo Zaidi wasiliana na mtafiti mkuu kwa njia ya barua pepe: skymuyuka@yahoo.com/0721948363 ama KNH-UoN kamati ya maadili na utafiti katibu: Profesa Mark Chindia, nambari ya simu +254207726300 ext. 44355, barua pepe: uonknh.erc@uonbi.ac.ke

APPENDIX 3: DATA COLLECTION TOOL

Code number of the participant……..

1. **Bio data.** What is the patient's bio data?

   Date of birth: Day…….Month…….Year……(Age)……..

   Sex: Male ☐ Female ☐

   Weight ---------- height---------- BMI----------

   Marital status:

   Single ☐ Separated ☐ Married ☐ Divorced ☐ Widowed ☐

2. **Types of drugs prescribed**

Current medication history: Prescription and Non-prescription medicines Allergies:					
Drug name	Type	Dosage	Frequency	Duration Start - stop	ADR reported

Past medication history (up to one month ago) : Prescription and non-prescription drugs					
Drug name	Type	Dosage	Frequency	Duration Start - stop	ADR reported
Home remedies/ herbal preparations/ dietary supplements/recreational drugs					
Drug name	Type	Dosage	Frequency	Duration Start - stop	ADR reported

3. **Social history.** What is the patient's social history?

   Occupation: Unemployed ☐ Self-employed ☐ Employed ☐ Retired ☐

   Income per month (Ksh):

   Education status: None ☐ Primary ☐ Secondary ☐ Tertiary ☐

   Religion: Protestant ☐ Catholic ☐ Muslim ☐ Traditional ☐ None ☐

   Alcohol intake: Yes ☐ No ☐

   Smoking: Yes ☐ No ☐

   Daily diet composition:

Regular Exercises: Yes ☐ No ☐

Investigations done six months prior to the study and during the study time

Test	**Value**	**Normal**	**High/Low**
Erythrocyte Sedimentation Rate			
C reactive protein			
Rheumatoid factor			
Anti-nuclear antibody (ANA) assay			
Anti-cyclic citrullinated peptide (anti – CCP)			
Anti- mutated citrullinated Vimentin (anti – MCV)			
Complete blood count: Red Blood Cells Hemoglobin Mean Corpuscular Volume Neutrophils Lymphocytes Monocytes Eosinophils			

4. Suspected adverse drug reactions reported by the patient

1. Do you you know the medicines you use for your illness? Yes/No

   If yes, which are they

2. Do you have trouble using your medicines? Yes/No

   If yes, briefly state their concerns in the space below.

3. Do the medicines make you feel unwell? Yes/No

   If yes, which of the following effects do you experience?

Adverse drug reaction	**Yes (1)**	**No (0)**
Nausea		
Vomiting		
Hair loss		
Pruritus		
Anorexia		
Weight loss		
Abdominal pain		
Fatigue		
urticaria		
Photosensitivity		
Diarrhea		

Fever		
Rash		
Respiratoryinfections		
Stomatitis		
Mucositis		
Tremor		
Infections		
Headache		
Hirsuitism		
Gum hyperplasia		
Female reproductive disorder		
Night sweats		
Cough		
Back pain		
Chills		
Asthenia		
Dizziness		
Injection site reaction		
Acne		
Delayed wound healing		
Diabetes mellitus		

Gastrointestinal perforation		
Insomnia		
Menstrual irregularity		
Osteoporosis		
Weight gain		
Edema		
Peptic ulcers		
Gastro intestinal bleeding		

APPENDIX 4: THE MORISKY MEDICATION ADHERENCE SCALE (MMAS-8)

Date:……..

Code of the participant…….

Question	Patient answer Yes/No	Score Yes = 1 No = 0
Do you sometimes forget to take your medicines?		
People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicines?		
Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?		
When you travel or leave home, do you sometimes forget to bring a long your medicine?		

Did you take all your medicines yesterday?		
When you feel like your symptoms are under control, do you sometimes stop taking your medicine?		
Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled a bout sticking to your treatment plan?		
How often do you have difficulty remembering to take all your medicine? A – Never/Rarely B – Once in a while C – Sometimes D – Usually E –All the time		A = 0 B – E = 1
TOTAL SCORE		

SCORES:

> 2 = Low adherence

1 or 2 = medium adherence

0 = high adherence

Reasons for non-adherence

Social and economic factors	**Yes**	**No**
Lack of finances		
Culture and beliefs about illness and treatment		
Family dysfunction		
Inadequate knowledge of treatment		
Condition related factors		
Level of disability		
Severity of the disease		
Availability of effective treatments		
Therapy related factors		
Duration of treatment		
Complexity of the medical regimen		
Frequent changes in treatment		
Adverse drug reactions		
Patient related factors		
Did not know that I had to take drugs daily		
Forgetfulness		
Anxiety of possible adverse effects		
Misunderstanding of treatment instructions		
Fear of dependence		
Hospital related factors		

Drug unavailable in the pharmacy		
Drug is unaffordable		
Concerns not addressed by clinician or other		
Instructions not clearly given to me		

APPENDIX 5: THE BRIEF PAIN INVENTORY TOOL
Date: ……

Code number of the participant……..

1. Throughout our lives, most of us have had pain from time to time such as headaches, sprains and toothaches. Have you had pain other than these everyday kinds of pain today?

   Yes ☐ No ☐

   If yes, how do you describe the pain?

   Mild ☐

   Moderate ☐

   Severe ☐

   Very severe ☐

2. What things make your pain feel worse?

3. What things make your pain feel better?

4. What treatments or medications are you receiving for your pain?

5. Please rate your pain by circling the one number that best describes your pain at its **WORST** in the past week.

   No pain 0 1 2 3 4 5 6 7 8 9 10 Worst pain you can imagine

6. Please rate your pain by circling the one number that best describes your pain at its **LEAST** in the past week.

   No pain 0 1 2 3 4 5 6 7 8 9 10 Worst pain you can imagine

7. Please rate your pain by circling the one number that best describes your pain on **AVERAGE**

   No pain 0 1 2 3 4 5 6 7 8 9 10 Worst pain you can imagine

8. Please rate your pain by circling the one number that tells how much pain you have **RIGHT NOW**

   No pain 0 1 2 3 4 5 6 7 8 9 10 Worst pain you can imagine

9. In the last week, how much relief have your pain treatments or medications provided? Please circle the one percentage that shows how much RELIEF you have received

   No relief 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% Complete relief

10. Circle the one number that describes how during the past week pain has interfered with your:

A. General activity

   Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

B. Mood

   Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

C. Walking ability

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

D. Normal work (includes both work outside the home and house work)

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

E. Relations with other people

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

F. Sleep

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

G. Enjoyment of life

Does not interfere 0 1 2 3 4 5 6 7 8 9 10 Completely interferes

Interference scale total scale: /70