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PREVALENCE AND IMPACT OF FIBROMYALGIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT THE KENYATTA NATIONAL HOSPITAL

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H58/34814/2019

MBChB

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF DEGREE OF MASTERS OF MEDICINE IN INTERNAL MEDICINE

Declaration

This dissertation is my original work and has not been presented for a degree in any other University

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Dedication

I dedicate this work to my family for their overwhelming support and inspiration.

Acknowledgements

I would like to express my deepest gratitude to my supervisors, Prof GO Oyoo, Prof J Kayima and Dr. Eugene Genga for their endless support and guidance throughout the study. I am also thankful to my research assistant Ms. Michele Kanago and the statistician Mr. Wycliffe Ayieko who made this work possible.

Finally, I would like to thank all the SLE patients who made this study possible.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

ACR -	American college of Rheumatology
ADL -	Activities of Daily Living
AZA -	Azathioprine
CBT -	Cognitive Behavioral therapy
CCC -	Comprehensive Care Centre
CNS -	Central Nervous System
CWP -	Chronic Widespread Pain
FDA -	Food and Drug Administration
FIQR -	Fibromyalgia Impact Questionnaire
fMRI -	Functional Magnetic Resonance Imaging
FMS -	Fibromyalgia Syndrome
HCQs -	Hydroxychloroquine
HIV -	Human Immunodeficiency Virus
HPA -	Hypothalamic Pituitary Adrenal axis
IBS -	Irritable Bowel Syndrome
KNH -	Kenyatta National Hospital
MOPC -	Medical Outpatient Clinic
PI -	Principal Investigator
QoL -	Quality of Life
RA -	Rheumatoid Arthritis
SLE -	Systemic Lupus Erythematosus

SLEDAI -	Systemic Lupus Erythematosus Disease Activity Index
SpA -	Spondyloarthritis
SPSS -	Statistical Package for Social Scientists
SSRI -	Selective Serotonin Reuptake inhibitor
SSS -	Symptom Severity Score
TCA -	Tricyclic Antidepressant
US -	United States
UK -	United Kingdom
UoN -	University of Nairobi
WPI -	Widespread Pain Index

Abstract

Background

Fibromyalgia is a medical condition mainly described by chronic widespread musculoskeletal pain (CWP), fatigue, and poor sleep. The association of fibromyalgia and lupus has been studied widely and it is conceivable that they may influence each other. The etiology of both the disease is unknown and the overlapping symptoms of lupus and fibromyalgia can lead to misinterpretation of lupus activity and risk of overtreatment. No studies of this association have been done in the black African population, bearing in mind the nature of the influence of chronic disorders on quality of life and disease activity. Understanding the nature of this association in our population may contribute to this discussion.

Objectives

To determine the prevalence and impact of fibromyalgia in patients with SLE attending the rheumatology clinic at the KNH.

Methodology

This is a cross-sectional descriptive study of SLE patients in Kenyatta National Hospital, rheumatology clinic. SLE patients with musculoskeletal pain were screened for fibromyalgia using the revised 2010 ACR criteria, those who fulfilled the criteria were diagnosed with fibromyalgia and subsequently given FIQR questionnaire to assess the severity of their symptoms. The activity of the disease was evaluated using SLEDAI-2K. A self-administered SF-36 form was used to evaluate the quality of life. Categorical data of the study population were summarized into proportions and continuous variables were summarized into means, medians, and SD. The prevalence of fibromyalgia is presented as a percentage. The severity of fibromyalgia was presented as a proportion in each class (mild, moderate, and severe). The QoL score was calculated and presented as proportions for good and poor. Disease activity was scored and classified into mild, moderate, and severe disease, and then presented into percentages.

Results

The study group comprised 60 patients, all women with a mean age of 34 years. The prevalence of fibromyalgia in patients with SLE was 65% (n= 39). All domains of HRQoL were impaired. The mean score of the 8 domains were; Physical function 30.6±19.2, physical health 3.2±8.5, emotional problems 15.4±36.6, fatigue 32.1±12.5, social function 39.5±16.3, emotional well-being 39.4±18.0, pain 39.7±12.7 and general health 30.6±19.2. The median SLEDAI score was 7.0 (IQR 4.0-10.0), with half of the patients having moderate–severe disease activity (51.3%). Patients with fibromyalgia were more likely to be on steroids than non-fibromyalgia (p-value < 0.05). Other factors like marital status, nature of employment, and age were found not to be statistically significant.

Conclusion

Fibromyalgia is prevalent in SLE patients presenting with chronic pain, in their middle age. The majority of the patients have moderate disease activity. The presence of fibromyalgia negatively impacts the quality of life of lupus patients.

1.0 Chapter One: Introduction

Fibromyalgia is mainly associated with chronic widespread musculoskeletal pain, deprived sleep, fatigue and cognitive disturbances (1). It's frequently accompanied by other inexplicable somatic symptoms and disability in activities of daily living (ADLs) (2,3).

The prevalence of FMS is correlated to both age and sex and it's estimated to be 2 to 4% in the general population. It's more common in women than men and advances in age (4).

Some factors (i.e. genetic and environmental) are known to predispose individuals to fibromyalgia, but the cause of fibromyalgia remains unknown. The most well-supported hypothesis in its etiopathophysiology is the alteration in the CNS function resulting in augmented nociceptive processing and the development of CNS-mediated symptoms of fatigue, impaired sleep, and cognitive disturbances (5). Functional neuroimaging studies and imbalance in the levels of excitatory and inhibitory neurotransmitters corroborates this phenomenon (6).

Fibromyalgia was first acknowledged and studied in the 16th century. In 1642 Guillaume de Baillou introduced the term "muscular rheumatism" and in 1904 W.R. Gowers coined the word "fibrositis" after attributing its pathophysiology to the fibrous tissue inflammation (7).

In 1976, P.K. Hench devised the term fibromyalgia as a form of non-articular rheumatism (8). In 1977, Smythe and Moldofsky continued the work of Hench and proposed a diagnostic criterion (9). They considered sleep disturbance and tender points to pain as the key features of fibromyalgia, which formed the foundation for the 1990 ACR diagnostic criteria of fibromyalgia (10).

The etiology of fibromyalgia remains unknown, however remarkable developments in the understanding of the disease have been made. It's postulated that both environmental and genetic factors are associated with fibromyalgia. Autoimmune, inflammatory, and infectious disorders have been attributed to the development of fibromyalgia.

Fibromyalgia can occur as either a primary disorder or concurrently with other distinct chronic diseases like rheumatoid arthritis, osteoarthritis, SLE, hypothyroidism, and Human Immunodeficiency infection (HIV) (11–14).

The burden of SLE has been on the rise over the recent years in our set-up, with 90% of patients presenting with musculoskeletal pain. This can be debilitating to patients who are already

suffering from lupus, hence it requires adequate assessment and management of the pain if successful therapy is to be achieved.

The association between fibromyalgia and SLE has been studied widely by various investigators with little clarity on their relationship (14–18). Both diseases have etiology of unknown origin, but it's conceivable that they may impact each other. The neuroendocrine regulation in fibromyalgia can affect the expression of lupus activity via the interactions of hormones with the immune system (19). Furthermore, both disorders present with similar dominant symptoms (i.e. arthralgia and fatigue) which can result in misinterpretation of lupus activity in an individual with both disorders.

There is a scarcity of data regarding the burden of fibromyalgia in SLE patients both locally and in Africa at large. Fibromyalgia usually leads to poor physical and social function, which can be incapacitating for many sufferers, thus negatively impacting the QoL of these patients who are already suffering from lupus. Fibromyalgia symptoms may also lead to misinterpretation of the lupus activity resulting in overtreatment in patients with both conditions. It is, therefore, significant to identify fibromyalgia with the sight to offer an appropriate mode of therapy to offer symptomatic relief.

2.0 Chapter Two: Literature Review

2.1 Epidemiology of Fibromyalgia

Fibromyalgia cases have been reported from all around the world, in all ethnic groups and cultures (20). Studies have shown that fibromyalgia is more common in females than males and higher in middle age (30-50 years) (21,22) or after 50 years of age (4,23). Wolfe et al reported an approximate prevalence of fibromyalgia at 2% in the American population which increases with age. They also found a higher female prevalence (3.5% in women and 0.5% in men) (4).

Branco et al also studied fibromyalgia in major European countries, he reported the prevalence of fibromyalgia to be 4.7% in rheumatology clinics and around 3% in the overall population. They also noted that the prevalence of fibromyalgia was related to both age and sex and varied among countries (23).

Locally, data on the prevalence of fibromyalgia is scarce; in 2011, Dokwe et al reported a prevalence of fibromyalgia in patients with chronic musculoskeletal pains attending the medical outpatient clinic (MOPC) at the KNH to be 11%, with middle-aged women contributing to more than 90% of the cases (24).

Mumo et al studied fibromyalgia at the Comprehensive Care Centre (CCC), KNH in HIV-positive patients. They found the prevalence of fibromyalgia syndrome to be at 18% and was higher disease activity compared to controls. They also noted that FMS was more predominant in females (25).

In 2019 Umar Jin's study at the diabetic clinic in KNH, documented a 28% prevalence rate of fibromyalgia in DM, predominantly in females (88%) with high disease activity (26). The recent report on fibromyalgia by Yego et al in patients undergoing hemodialysis found that 18% of the patients had fibromyalgia and they were six times more prone to have poor QoL than controls (27).

Racial differences have been seen in the US, where there was a higher prevalence of fibromyalgia in black American women than in white (28). However, poor socio-economic status is associated with augmented bodily pain and tenderness, hence this might be a significant influence on racial differences.

Gender differences were also reported in some clinical features where men with fibromyalgia are likely to have a lesser insight into health and more physical limitations, in contrast to the women who have increased pain sensitivity and might demonstrate greater life restriction because of the pain than the males (29).

2.2 Etiology and Pathophysiology

Fibromyalgia is a chronic pain condition of unknown etiology and indistinct pathophysiology. Environmental factors including certain infections, together with emotional or physical trauma might trigger and/or aggravate symptoms of fibromyalgia. Several observational and biological studies have suggested that genetic predisposition may also be a factor in the etiopathology of fibromyalgia (30).

Fibromyalgia is presently comprehended as a central sensitization syndrome or a central pain processing disorder. Central sensitization refers to a state wherein the CNS amplifies sensory input across multiple organ systems resulting in myriad symptoms (31). At the cellular level, there is an alteration in the systemic processing of pain and functional connectivity in the brain (6).

Emerging evidence suggests that there is pain processing dysfunction in fibromyalgia syndrome, where there is a mismatch between excitatory (substance P, glutamate) and inhibitory neurotransmitter (serotonin, norepinephrine) concentrations (32).

Apart from the genetic and environmental factors, functional magnetic resonance imaging (fMRI) has significantly advanced the field. In response to nociceptive stimuli, multiple imaging studies of the brain have described an augmented pain processing activation in fibromyalgia. This indicates the existence of a hyperactive detection of pain and processing system (33–35). Further studies have proven that patients with fibromyalgia have reduced activation and connectivity in the inhibition of pain (36).

Sleep disturbance is considered an intrinsic feature of fibromyalgia. The intrusion of alpha-wave into the delta-wave stage IV sleep has been reported as a sleep anomaly in fibromyalgia. This intrusion causes the patient to arouse to a lighter sleep level (37).

2.2.1 Pathogenetic Theories

1) **CNS altered pain processing**

Alteration in the processing of pain in the CNS is responsible for many of the key features of fibromyalgia. The following mechanisms have demonstrated fibromyalgia as a disorder of pain processing:

- Temporal summation of pain – patients with FMS experience greater than normal pain intensity after administering a rapidly repetitive noxious stimulus (38,39).
- Reduced endogenous pain inhibition – There is a deficiency of endogenous analgesic systems in fibromyalgia. Following repetitive nonpainful stimuli, there is a reduction in both inhibitory control of diffuse noxious stimuli and a failure to inhibit irrelevant stimuli (40,41).
- Pain receptors and pain-related neuropeptides – Upregulation of the peripheral opioid receptors and a decline in the brain are observed. Substance P is increased in the CSF compared with controls (42).
- Brain neuroimaging – Brain imaging studies demonstrate pain dysregulation in FMS.

2) **Genetic Predisposition**.

Fibromyalgia is highly aggregated in families of patients with fibromyalgia. A study done by Arnold et al ascertained that there is the involvement of genetic factors in the etiology of FMS, the mood disorders and fibromyalgia are more prone to share such inherited factors. They observed that the first-degree relatives of fibromyalgia patients are likely to develop FMS 8 times more than the controls (43).

In another study among blood relatives of fibromyalgia patients, the prevalence of FMS was found to be around 26% in contrast to 19% among their husbands (44). This higher prevalence of fibromyalgia was attributed to genetic factors.

3) **Serotonin**.

Serotonin is a key neurotransmitter in the CNS; it plays a major function in pain perception, sleep cycle, anxiety, and depression. Abnormally low serotonin levels have been widely associated with fibromyalgia (45).

4) **Immune Abnormalities**.

The role of cytokines in the pathophysiology of fibromyalgia is still unknown. Eligible studies have revealed that patients with fibromyalgia have higher serum concentrations of Interleukin-1, 6, and 8 compared with controls.

5) **Stress/Autonomic Nervous System (ANS) Dysfunction.**

Patients with FMS are associated with dysfunction in the autonomic nervous system, consistent with overactivation of the sympathetic system. Pain increases the activation of sympathetic cardiac activity, and reduces sleep efficiency causing lighter sleep (46).

6) **Infection and Vaccination**

Certain infectious agents like Covid-19, HIV, Lyme disease, and Hepatitis C have all been associated with fibromyalgia and may trigger or aggravate the symptoms (47,48).

Some data have postulated the possible vaccine's role in triggering the development of fibromyalgia, but this association remains to be proven.

7) **Substance P**

When the axons are stimulated substance-P neurotransmitter is released. Higher substance-P levels raise the nerve sensitivity to pain, thus intensifying pain awareness. Studies have revealed that fibromyalgia patients have higher than normal substance P levels in their CSF, which results in exaggerated nociception (42).

8) **The hypothalamic-pituitary-adrenal axis (HPAA)**

Neuroendocrine functional studies have reported HPA axis dysfunction in fibromyalgia patients (49). In a study among females with fibromyalgia and chronic fatigue, they were found to have low levels of cortisol and growth hormone compared to controls (50).

2.3 Diagnosis of Fibromyalgia

Establishing the diagnosis of FMS is necessary for effective management. In contrast to the initial 1990 ACR diagnostic criteria of fibromyalgia, the preliminary 2010 ACR criteria of fibromyalgia do not necessitate examination of a tender point, it provides a measuring scale of symptoms severity that are distinctive of fibromyalgia (51).

The current guideline no longer recommends palpating specific "tender point" areas but rather estimates widespread soft tissue tenderness. To design diagnostic criteria for FMS, it gradually became apparent to clinicians that the tender point examination, an important element of the 1990 criteria, should not be used for the diagnosis of fibromyalgia and that the presence of somatic symptoms like sleep disturbances and fatigue must be included in the diagnostic criteria.

Fibromyalgia is diagnosed based on symptoms of CWP in various sites and is commonly accompanied by fatigue and sleep disturbance. The patient satisfies the diagnostic criteria of fibromyalgia if the following parameters are met:

1) The widespread pain index (WPI) is more than 7 and the symptom severity scale (SSS) of more than 5 or a WPI of between 3 - 6 and an SSS of more than 9.
2) Presence of symptoms for a duration of 3 months.
3) Exclude other conditions that may describe the patient's symptoms.

The WPI quantifies the number of painful areas of the body from a defined list of nineteen regions. It measures the degree of pain on a gauge of 0 to 19 by asking the patients if they had experienced any pain or tenderness in nineteen different areas (Figure 1), each painful/tender body area scoring 1 point.

The symptom severity score (SSS)- tends to evaluate the degree of severity of the 3 cardinal symptoms of fibromyalgia (i.e. daytime fatigue, deprived sleep, and cognitive disturbances) and other somatic symptoms on a scale of 0 (lowest intensity) to 12 (highest intensity of symptoms).

Figure 1: Regions for scoring of widespread pain index

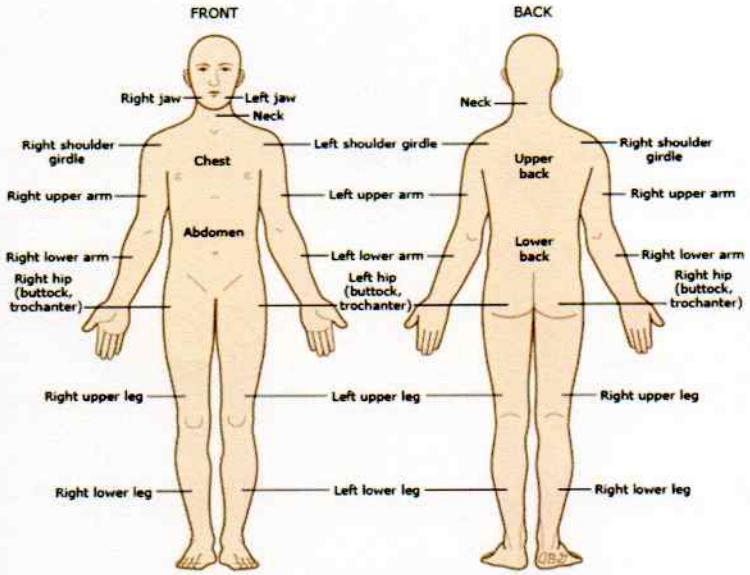


Table 1: Measurement of symptom severity of Fibromyalgia

SS scale score:
A) For the each of the following symptoms below, indicate the level of severity over the past 7 days using the following scale:
0 = no problem
1 = slight or mild problems, generally mild or intermittent
2 = moderate, considerable problems, often present and/or at a moderate level
3 = severe: pervasive, continuous, life-disturbing problems
- Fatigue (0-3)
- Waking unrefreshed (0-3)
- Cognitive symptoms (0-3)
B) How many of the following had the patient had in the past 6 months?
(1) Headaches (0–1)
(2) Pain or cramps in lower abdomen (0–1)
(3) And depression (0–1)
The symptom severity scale (SSS) score: Sum of the total severity scores of the symptoms in group A (0-9) and B (0-3) above. The final score is between 0 and 12

2.3.1 The Fibromyalgia Impact Questionnaire (FIQR)

A validated modified tool for assessing the health status of patients with fibromyalgia (52). The revised FIQR is divided into three main set of domains used to assess: (a) The function (b) Overall impact and (c) The intensity of fibromyalgia symptoms.

The FIQR consist of 21 individual questions, rated from 0 to 10 (with 10 being worse) on an 11-pointer numerical scale.

2.3.2 Scoring System of FIQR

Three domains (functional, overall impact, and intensity of symptoms) are scored independently on a scale of zero to ten. Eleven boxes in the questionnaire denote the numbers 0-11 from left to right.

Step 1: Sum the scores of each of the three domains.

Step 2: Divide the summed score of domain 1 (range 0-90) by 3

Divide the summed score of domain 2 (range 0-20) by 1

Divide the summed score of domain 3 (range 0-100) by 2

Step 3: The total score of FIQR is obtained by adding the 3 domains above in step 2 (ranging from 0 to 100)

2.4 Impacts of FMS

FMS has a greater impact on the utilization of both healthcare and non-healthcare resources. Screening and diagnosing of fibromyalgia will result in a reduction in resources use, including subsequent testing and the burden of health care costs. Hughes et al reported that throughout the 10 years prior to diagnosing fibromyalgia, patients had a higher annual rate of visits, diagnostic procedures, testing, and medication prescription compared to controls (53).

Fibromyalgia can affect a patient's relationship with other people in the community including family members and workmates. Pain and cognitive symptoms may impact on the productivity of people living with fibromyalgia leading to stigmatization and lack of social acceptance by the community.

In a study of female patients with fibromyalgia, it was discovered that women feel imprisoned by the illness and undergo a psychosocial process of "struggling to maintain balance" i.e. in recalling perceived normalcy, probing for diagnosis, depleting resources, and even relinquishing the struggle (54).

2.5 Chronic Widespread pain and Rheumatologic Conditions

Patients with rheumatic conditions despite having localized pain from the primary disease, also experience chronic widespread pain (CWP) similar to those with FMS.

Central pain is a significant mechanism in FMS and related chronic pain disorders, it refers to any pain that cannot be explained by a peripheral source (55). 10-40% of patients with rheumatic disorders like SLE, osteoarthritis, psoriatic arthritis, Spondyloarthritis (SpA), and rheumatoid arthritis are estimated to present with centralized pain.

Chronic pain in rheumatic disorders results from the overlapping of central pain with other pain categories including inflammatory, structural, and neuropathic to some degree. Chronic widespread pain, a cardinal symptom of fibromyalgia is determined in defining pain in FMS using five quadrants of the body i.e. the upper and lower limb on each body side and the axial skeletal.

The clinical and imaging finding of chronic widespread pain (CWP) with centralized pain are common in rheumatic disease patients. The presence of concomitant CWP/FMS, seen in a quarter of patients with osteoarthritis, inflammatory joint disorders and chronic backache may enhance the patient's pain level and other somatic symptoms, potentially affecting the measurement of disease activity, and altering treatment decisions and therapy outcomes.

Fibromyalgia in rheumatoid arthritis was linked with higher disease activity, poorer outcomes, and greater medication burden compared to their counterpart. Fibromyalgia is estimated to be prevalent in rheumatoid arthritis at 12-40% (56,57).

FMS is also more prevalent in chronic inflammatory arthritis than in the general population and may impact the disease activity and management of these patients (58). Patients with fibromyalgia were found to have a higher burden of the disease and poorer response to therapy. In a study to establish the occurrence of fibromyalgia in patients with spondyloarthritis, 20.7% of the patients had fibromyalgia and were associated with significantly worse disease activity, higher number of disability and psychological comorbidities, poor QoL, and greater impact on work than the control (59). Patients with fibromyalgia were found to experience work impairment in half of their working time with a greater percentage of work time missing.

2.6 SLE and Fibromyalgia

SLE is a multisystem autoimmune disease of unknown cause, it can affect any organ in the body. Globally, the prevalence of SLE is reported to range widely from 20-150 cases per 100,000, and is predominantly in women, in their reproductive age (60,61).

In Africa, SLE was thought to be less common, however recent studies have shown an increase in the prevalence of SLE among black Africans (62,63). In Kenya, the rise in the number of SLE cases over the recent years has been associated with poor QoL, disability, and health care cost burden (64–69).

In 2016, Nyambane et al assessed the activity of disease and HRQol in patients with SLE at the KNH, she reported a poorer QoL in younger age, newly diagnosed lupus and those with renal disease. Majority of the patients had moderate-severe disease activity (69).

Data from the United Kingdom (UK) has shown that 85% of SLE patients present with musculoskeletal manifestations (70). In 2015, a local study by Genga et al also documented that 90% of patients with lupus manifest with musculoskeletal pain (64).

Chronic musculoskeletal pain, the main feature of FMS has been studied in patients with lupus. The incidence of fibromyalgia in SLE has been the subject of discussion by several investigators and it is estimated to be between 8 to 61%.

A study done by Middleton et al in Texas, where he investigated 102 patients with SLE in the lupus clinic, demonstrated that FMS was prevalent in 22% of the patients. The other 23% had clinical features suggestive of fibromyalgia, but did not meet the criteria of fibromyalgia and were referred to as probable FMS (PFMS) (14). In the study, fibromyalgia was not only common in lupus, but a primary determinant of the severity of symptoms and incapacity.

Wolfe et al, studied 23,231 adults with rheumatic disease, of which 834 had SLE. The results revealed that 22% of SLE patients had fibromyalgia compared to 17% of those with arthritis (Rheumatoid arthritis and non-inflammatory rheumatic disease) (17). Fibromyalgia in lupus patients was associated with higher disease activity in contrast to their control.

In 2013 a study done by Luiza et al in Brazil to establish the frequency and impact of fibromyalgia in SLE patients reported that 12% of the patients had fibromyalgia between 40-44 years of age. It was noted that fibromyalgia poorly affects the QoL of lupus patients (18).

Another study from Israel reported that the QoL in SLE patients was negatively impaired by fibromyalgia compared to controls, and better control of fibromyalgia will result in improvement in QoL in SLE patients (71).

In Canada, Gladman et al reported the prevalence of fibromyalgia to be around 22% in 119 lupus clinic patients. They reported that FMS is a major contributor to poor QoL in patients with lupus (15). Another study by Buskila et al revealed that fibromyalgia syndrome is not only prevalent in patients with lupus but also a cause of disability. He noted that fibromyalgia negatively impairs the QoL of patients with lupus, and some clinical presentations of fibromyalgia may result to misinterpretation of lupus activity (72).

In an Indian tertiary referral center, 158 patients with SLE were studied and 13 patients (8.2%) were found to have FMS (73). The low prevalence was attributed to a strong family support system, racial variations in the threshold of pain and/or the virtual lack of disability benefits. Finally, Morand et al reported 22 (25.3%) all female, the prevalence of fibromyalgia among 87 patients with SLE (74). The presence of fibromyalgia has a substantial adverse effect on the QoL of patients living with lupus.

2.6.1 Assessment of Disease Activity in SLE

In patients with SLE, the activity of the disease is estimated by the degree of organ involvement or by the serological activity.

SLEDAI was developed in 1985 by an experienced panel of rheumatologists in Toronto, Canada. SLEDAI was initially used as a tool to standardize and measure the disease activity in lupus in the preceding 10 days. It assesses 24 clinical and laboratory variables linked with SLE activity, aggregated into 9 organ systems which are weighed differently with values ranging from 1 to 8 i.e. CNS and vascular systems can each score to a maximum point of 8, renal and musculoskeletal structures can each score to a maximum of 4 points. Skin, serous and immunological system can each score a maximum of 2 points, hematological and constitutional systems can each score a maximum of 1 point. The overall score ranges from 0-105, with the higher values correlating to higher disease activity.

In 2002, a modified version of SLEDAI was introduced and it included persistent active disease (rash, mucosal membrane ulcers, alopecia, and proteinuria) in the variables (75). SLEDAI-2K has been displayed to be a stronger predictor of mortality and organ damage.

2.6.2 Health-Related Quality of life (HRQoL)

A complex notion that portrays the general perception of the patient on the impact of the disease and its therapy on their physical, social, and emotional function.

Quality of life (QoL) can be evaluated using either a generic tool (SF-36) or a specific disease tool (LUPUSQoL). The generic measure is a widely used tool in examining HRQoL in SLE patients, it allows comparison of the HRQoL in SLE to other related conditions or population norms (76).

The 36-Item Short Form is a validated generic tool used in assessing the quality of life. It's composed of 36 questions which are grouped into 8 main domains with each subscale i.e. general health wellbeing, physical function, role limitation due to physical health, pain, mental health, social functioning, vitality/energy, and emotional role limitation. Each item has a scoring scale ranging from 0 to 100.

2.7 Management of FMS

FMS is often difficult to treat, it requires a multidisciplinary, individualized treatment approach that incorporates the primary clinician and other healthcare experts in physical medicine, rehabilitation, and mental health.

Effective interventions entail both non-pharmacologic and pharmacologic therapies. Different drugs classes have been approved by the FDA for fibromyalgia:

i. Selective serotonin reuptake inhibitors (SSRIs) - fluoxetine
ii. Serotonin and norepinephrine reuptake inhibitors (SNRIs) - milnacipran, duloxetine
iii. Tricyclic antidepressant (TCA) - amitriptyline
iv. Anticonvulsant (pregabalin)

There is evidence that dual therapy of different drug classes results in significantly greater improvement in pain compared to monotherapy (77,78).

Other agents such as acetaminophen, tramadol, and NSAIDs are adjunctive or alternative therapies in patients with a temporary need for additional treatment during an exacerbation of pain.

Non-pharmacological intervention includes patient education, exercise (water-based or aerobic), strength training, meditative movement therapies (yoga, tai chi, qigong), and psychological therapy like cognitive behavioral therapy (CBT).

2.8 Problem Statement

Fibromyalgia has remarkably adverse effects on both the physical and psychosocial health of affected individuals, especially in patients with other chronic diseases such as lupus (53). Pain and cognitive symptoms in fibromyalgia may affect the productivity of people living with fibromyalgia leading to stigmatization and lack of social acceptance by the community.

Fibromyalgia symptoms may also lead to misinterpretation of the lupus activity and influence treatment decisions in patients with both conditions. It is, therefore, significant to identify this condition with the sight to offer an appropriate mode of therapy to alleviate the suffering.

In Kenya, the prevalence and impact of fibromyalgia in SLE have not been studied despite the studies showing that more than 80% of patients with lupus present with musculoskeletal manifestations (64,70). Without such information, the burden of fibromyalgia in SLE patients with musculoskeletal pain will never be understood.

2.9 Study Justification

The burden of SLE has been on the rise in rheumatology clinics over recent years. In Africa, the prevalence and incidence of SLE are still unclear, however, a report by Oyoo et al revealed an increase in the prevalence of lupus in native populations of Eastern, Central, and South Africa (79).

Chronic widespread pain (CWP), the cardinal symptom of fibromyalgia is known to cause morbidity and disability, which can be debilitating. The pain, fatigue, and deprived sleep seen in fibromyalgia can negatively affect the QoL and impairs the productivity of patients with lupus. Studies have shown that fibromyalgia is not only common in patients with lupus, but the main determinant of the frequency and severity of symptoms, furthermore fibromyalgia causes incapacity for daily activities (14), thus better control of fibromyalgia will lead to an improvement in the QoL of patients with lupus.

There is also a scarcity of data on the burden of fibromyalgia in patients with lupus, both locally and in Africa at large. Most of the existing data are from America, Europe, and Asia, this study will fill the knowledge gap.

The drive of this study is to determine the prevalence and impact of fibromyalgia on QoL and disease activity in SLE patients, to sensitize the clinical personnel on its occurrence.

2.10 Research Question

What is the burden and impact of fibromyalgia in SLE patients with chronic musculoskeletal pain on follow-up at the Kenyatta National Hospital, rheumatology Clinic?

2.11 Broad Objective

To establish the prevalence and impact of fibromyalgia in SLE patients with chronic pain at the rheumatology clinic, KNH.

2.12 Specific Objectives

1) To determine the prevalence of fibromyalgia in SLE patients with chronic pain.
2) To determine the severity of fibromyalgia-related symptoms using FIQR tool.
3) To establish the impact of fibromyalgia on the quality of life in patients with SLE using SF-36 form.
4) To establish the impact of fibromyalgia on the disease activity in SLE patients using the SLEDAI-2K index.

3.0 Chapter Three: Methodology

3.1 Study Design

Cross-sectional descriptive study

3.2 Study Site

The Kenyatta National Hospital is the biggest teaching and referral hospital in Eastern and Central Africa, with a bed capacity of more than 2000. It is situated in Nairobi, Kenya. The Rheumatology clinic is one of the busiest and largest outpatient clinics in the country, it runs every Tuesday and Thursday from 2 to 5 pm seeing almost 60 patients per day. The clinic is attended by consultant rheumatologists and resident doctors from the Department of Internal Medicine and Pediatrics.

3.3 Study Population

SLE patients with chronic musculoskeletal pain on follow-up at the rheumatology clinic.

3.4 Patient Selection

3.4.1 Inclusion Criteria

i. Patients with a diagnosis of SLE
ii. Patients above 15 years of age
iii. Patients who give informed written consent and assent for patients < 18 years
iv. Patients with chronic musculoskeletal pain >3 months

3.4.2 Exclusion Criteria

1) Patients who are not able to give a proper description of symptoms.

3.5 Sample Size Estimation

The sample size was estimated using Fisher's equation:

$$n = \frac{Z^2 p(1-p)}{d^2}$$

n – Minimum sampling size
z – Normal deviant =1.96 (95% confidence interval)
p – Prevalence value of fibromyalgia in SLE by Middleton et al in the US (22%)
e – Margin of error (precision error) = ±5 %.

$$n = \frac{(1.96)^2 \times 0.22\ (1-0.22)}{(0.05)^2}$$

The minimum sample size is 264

The prevalence was derived from a study by Middleton et al in the US, where the prevalence of fibromyalgia was found to be 22% in SLE patients (14). This study was used since it directly evaluates the prevalence and impact of fibromyalgia in patients with SLE.

However, according to the data from KNH records a total number of 77 patients with lupus were on follow-up at the rheumatology clinic between Jan-Dec 2020. Since the sample size exceeds the total population, the corrected Fishers formula based on the finite population (N< 10,000) will be:

$$nf = n/(1+n/N)$$

nf = new sample size where the population <10,000

n = desired sample size calculated using the Fishers formula

N = Total study population

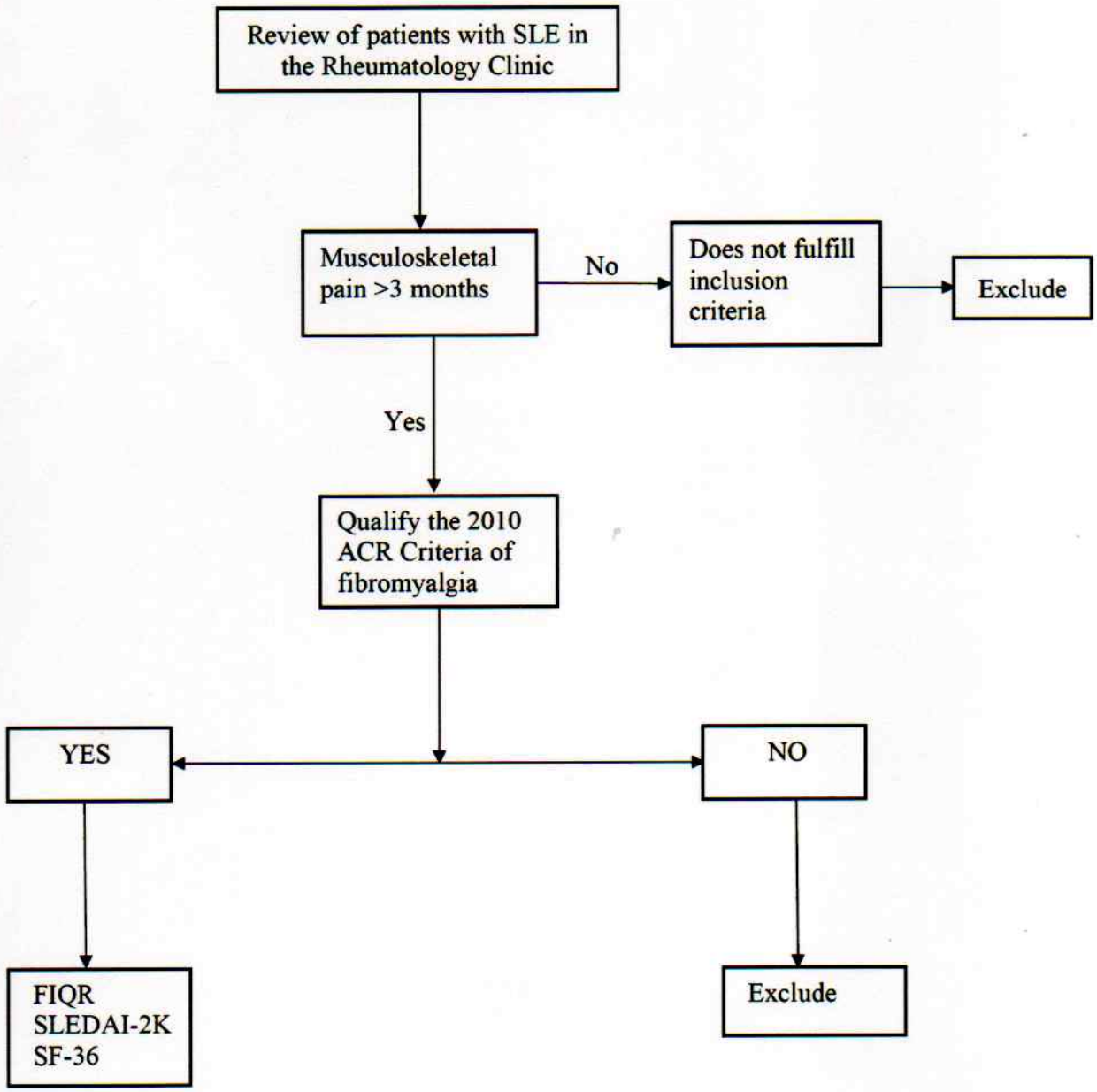
$$nf = \frac{264}{1+264/77} \qquad nf = 60$$

A minimum of 60 patients is required to determine the prevalence of fibromyalgia in SLE with a 5% margin of error.

3.6 Sampling Procedure

A consecutive sampling method was utilized until the desired sample size was achieved. Participant recruitment was done by the principal investigator (PI). The PI visited the rheumatology clinic every Tuesday and Thursday between 2-5 pm and reviewed the patient's files. All the patients with a file diagnosis of SLE who qualified were enrolled in the study.

Figure 2: Flow Chart for Patient Recruitment



3.7 Data collection and Clinical Methods

3.7.1 Data Collection Tools

1) The revised Fibromyalgia Impact Questionnaire (FIQR): Was used to evaluate three sets of domains of fibromyalgia i.e. the function, impact, and intensity of fibromyalgia symptoms (52).
2) The SLE Disease Activity Index (SLEDAI-2K): Was used to assess the activity index of SLE and the impact of fibromyalgia on SLE. It assessed 24 clinical and laboratory variables associated with SLE activity.
3) SF-36 questionnaire: Generic questionnaire used to evaluate the QoL in SLE patients. It assesses 8 health concepts.
4) Widespread Pain Index (WPI): Was used to evaluate the extent of pain in 19 different body regions on a scale of 0-19.
5) Symptom severity Scale (SSS): It evaluated the degree of severity of the main symptoms of fibromyalgia (except pain) on a scale of 0-12.

   Both WPI and SSS comprise the preliminary 2010 ACR criteria for fibromyalgia.

3.7.2 Data Collection Methods

The following sequence of data collection was followed:

i. Informed consent was obtained and a structured screening proforma was administered by the primary investigator (Appendix 6).
ii. The patients who qualified for the inclusion criteria were enrolled. The study questionnaire was then administered to the patients (Appendix 7). Clinical history and demographic data were retrieved from the patient's file.
iii. The 2010 ACR diagnostic criteria was used to establish cases of CWP and fibromyalgia. Widespread pain index (WPI) was obtained by modest palpation of multiple soft tissue sites and asking the patient if they had experience pain/tenderness in the preceding 7 days.
iv. The severity of the 3 main symptoms of fibromyalgia and other somatic symptoms were evaluated using the symptom severity score (SSS).
v. Those who satisfied the 2010 ACR criteria were diagnosed to have fibromyalgia and FIQR tool (appendix 8) was administered to assess the severity and impact of fibromyalgia.
vi. A comprehensive physical examination was conducted by the PI evaluating the skin, scalp, presence of mucosal ulceration, signs of vasculitis, and a targeted systemic

examination i.e. neurological, cardiovascular, respiratory and musculoskeletal system. An ECG was done after the completion of clinical examination.

The clinical variable of SLEDAI-2K (appendix 9) was completed after verification of the findings with the consultant rheumatologist.

vii. Patients were given an SF-36 questionnaire (appendix 10) which was preferentially self-administered. For those in need of assistance, the PI filled out the form after reading the question and the patient responded.

viii. An aseptic technique was used to take blood samples (full blood counts, creatinine kinase) for evaluation. Urine sample bottles were given to patients to collect a clean catch sample for urinalysis.

3.8 Study Variable

3.8.1 Independent Variables

1. Age: Documented as the number of years written in the file or reported from the birth date.
2. Sex: Categorized as either male or female
3. Marital Status: Recorded as single, married, divorced, or widowed.
4. Level of education: The highest education level achieved by the patient.
5. Duration of disease: Time interval from the first time the diagnosis was confirmed to the last follow-up.
6. Treatment modality: Defined as the current drug use, duration, and dosage. Drugs were classified as NSAIDs, steroids, DMARDs, and antimalarial.

3.8.2 Dependent Variables

1. The prevalence of fibromyalgia
2. The Impact of fibromyalgia on quality of life in SLE patients.
3. The impact of fibromyalgia on disease activity in SLE patients.

Outcome Variables

1. **Quality of life**

The Quality of life was evaluated using a generic SF-36 tool. It consists of 8 domains with each subscale including physical functioning (10 items), general health perception (5 items), emotional well-being (5 items), role limitation due to physical health (4 items), social functioning (2 items), pain (2 items), the energy (4 items) and emotional role (3 items). Each item is scored in a range of 0 (worst QoL) to 100 (better QoL).

Scoring System of SF-36

Scoring of the SF-36 questionnaire involves two main steps:

1- All 36 items are scored and converted to a scale ranging between 0-100, with a higher score representing a more favorable self-perceived QoL.

2- Average all the answered items together on the same scale to form an 8-scale score. Unanswered items are not considered when calculating the scale scores.

2. **Disease Activity**

SLEDAI-2K was used to assess the disease activity in patients with lupus. 24 clinical and laboratory variables associated with SLE activity were assessed and further categorized into three major groups:

a) Mild disease activity (0-5)
b) Moderate disease activity (6-12)
c) Severe disease activity (>13)

Table 2: Assessment of Disease Activity in SLE

Weight	SCORE	Descriptor	Definition
8	❒	Seizure	Recent onset, exclude metabolic, infectious or drug causes.
8	❒	Psychosis	Altered ability to function in normal activity due to severe disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Exclude uremia and drug causes
8	❒	Organic brain syndrome	Altered mental function with impaired orientation, memory, or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious, or drug causes.
8	❒	Visual disturbance	Retinal changes of SLE. Include cytoid bodies, retinal hemorrhages, serous exudate or hemorrhages in the choroid, or optic neuritis. Exclude hypertension, infection, or drug causes.
8	❒	Cranial nerve disorder	New onset of sensory or motor neuropathy involving cranial nerves.
8	❒	Lupus headache	Severe, persistent headache; may be migrainous, but must be nonresponsive to narcotic analgesia.
8	❒	CVA	New onset of cerebrovascular accident(s). Exclude arteriosclerosis.
8	❒	Vasculitis	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, or biopsy or angiogram proof of vasculitis.
4	❒	Arthritis	$\geq$ 2 joints with pain and signs of inflammation (i.e., tenderness, swelling or effusion).
4	❒	Myositis	Proximal muscle aching/weakness, associated with elevated creatine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis.
4	❒	Urinary casts	Heme-granular or red blood cell casts.
4	❒	Hematuria	>5 red blood cells/high power field. Exclude stone, infection or other cause.
4	❒	Proteinuria	>0.5 gram/24 hours
4	❒	Pyuria	>5 white blood cells/high power field. Exclude infection.
2	❒	Rash	Inflammatory type rash.
2	❒	Alopecia	Abnormal, patchy or diffuse loss of hair.
2	❒	Mucosal ulcers	Oral or nasal ulcerations.
2	❒	Pleurisy	Pleuritic chest pain with pleural rub or effusion, or pleural thickening.
2	❒	Pericarditis	Pericardial pain with at least 1 of the following: rub, effusion, or electrocardiogram or echocardiogram confirmation.
2	❒	Low complement	Decrease in CH50, C3, or C4 below the lower limit of normal for testing laboratory
2	❒	Increased DNA binding	Increased DNA binding by Farr assay above normal range for testing laboratory.
1	❒	Fever	>38° C. Exclude infectious cause.
1	❒	Thrombocytopenia	<100,000 platelets / x10^9/L, exclude drug causes.
1	❒	Leukopenia	< 3,000 white blood cells / x10^9/L, exclude drug causes.
TOTAL SCORE	_____		

3.9 Quality Assurance

The existing hospital protocol and the standard operating procedures were strictly adhered to at all times during the study. The study tools have been used worldwide and have been validated in different languages. They were translated into Kiswahili for the ease of the patients, and have been previously used in various studies at the KNH. Training of research assistants was done prior to data collection.

3.10 Data Management

3.10.1 Data Handling

Data were collected during the rheumatology clinic visits. Details about SLE (duration of the disease, current medication, and any end organ damage) were retrieved from the file. Completed data were locked in a secure cabinet by the PI for analysis.

3.10.2 Data Analysis and Presentation

Data were entered and managed in Microsoft Excel 2016 spreadsheet. Cleaned data was exported to SPSS version 23.0 for statistical analysis. The study population was described by summarizing socio-demographic and clinical characteristics into percentages for categorical data; for continuous variables mean and SD was used for normally distributed data, while median and IQR were for skewed data.

The prevalence and severity of fibromyalgia were determined and presented as a proportion of all SLE patients studied. Quality of life (QoL) score was calculated using the SF-36 scoring tool and presented as proportions for good and poor.

SLE disease activity was scored and SLEDAI-2K tool cut-offs were used to categorize patients into mild, moderate, and severe diseases then presented using percentages.

Socio-demographic features and clinical history of the patients were associated with fibromyalgia using the chi-square test.

Odds ratios were calculated and presented as estimates of the risk of fibromyalgia associated with each of the exposure variables. Statistical tests were interpreted at a 5% level of significance. Results are presented in the form of charts and tables.

3.11 Ethical Consideration

This study was carried out after consent from the Department of clinical medicine and Therapeutics, University of Nairobi (UON), the KNH/UON scientific and ethical research committee. Patients who qualified to participate in the study were enrolled after giving informed written consent or assent.

Patients were educated on the objectives and purpose of the study in their convenient language prior to recruitment. Patients were guaranteed that participation was voluntary and there was no victimization to those declining to participate. Patients were guaranteed free and full access to their results. Those diagnosed with fibromyalgia were offered therapy. Patient discretion was strictly maintained and all the information collected was stored safely under lock and key.

4.2 Demographic and Social characteristics of patients

The mean age of the patients was 33.55 years (SD 7.61), where the minimum age was 16.0 years, and the maximum was 52.0 years. The median age was 34.0 (IQR 29.0 – 38.0) years. The entire respondent in the study were females (60). Thirty-four (34) (56.7%) were married, 1 (1.7%) was separated from the spouse and 25 (41.7%) were single at time of recruitment. About 47 patients (78.3%) reported that they were involved in activities that did not require any manual form of labor, while 13 (21.7%) reported engaging in manual activities during their daily activities. Thirty-four patients (56.7%) were unemployed at the time of study and 26 (43.3%) were employed. A total of 54 (90%) study participants had post-primary education.

Table 3: Sociodemographic characteristics of the study population

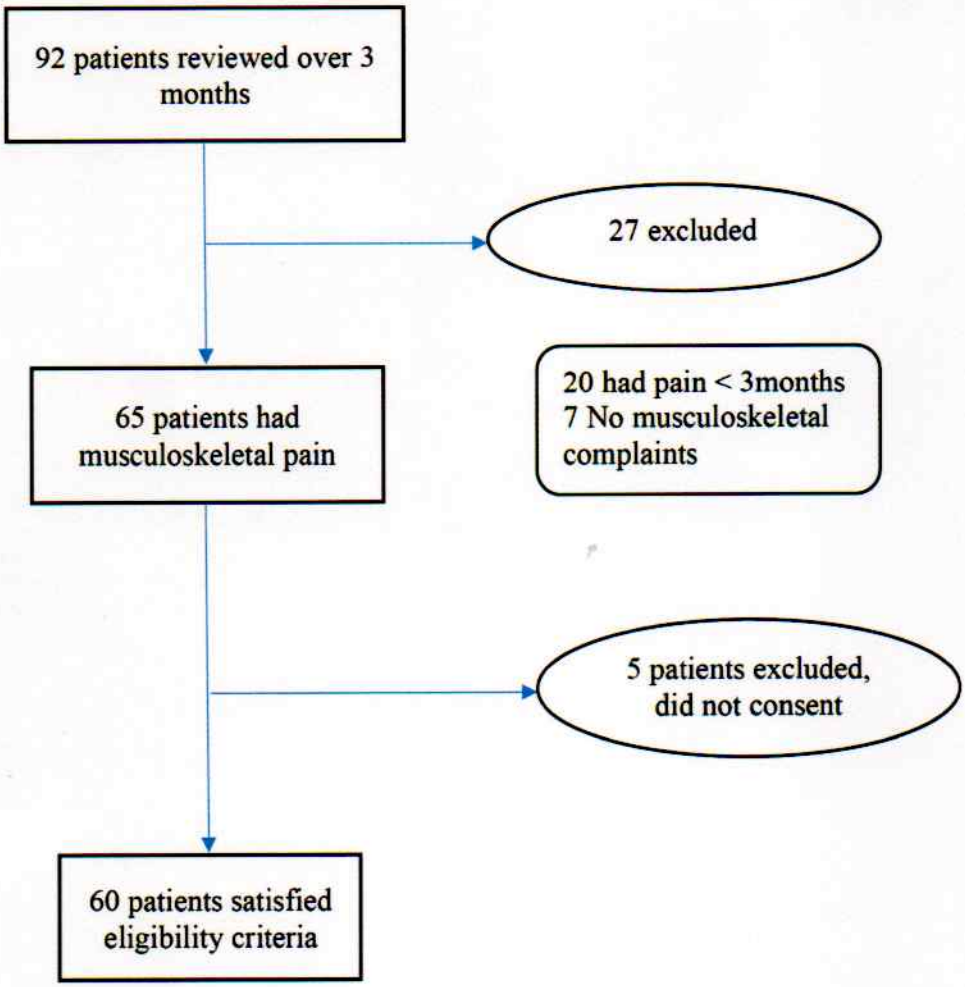
Variable	Frequency, *n=60*	Percentage
Age in years		
< 20	2	3.3
20 – 29	15	25.0
30 – 39	33	55.0
40 – 49	7	11.7
50 – 59	3	5.0
Marital Status		
Single	25	41.7
Married	34	56.7
Divorced/Separated	1	1.7
Educational Level		
Primary	6	10.0
Secondary	29	48.3
Tertiary	25	41.7
Daily activities		
Manual	13	21.7
Non-manual	47	78.3
Occupation		
Employed	26	43.3
Unemployed	34	56.7

4.0 Chapter Four: Results

4.1 Patient Recruitment

A total of 92 patients with SLE attending the rheumatology clinic were assessed for chronic musculoskeletal pain between July and October 2022. Of these, 27 patients did not qualify the inclusion criteria and 5 patients declined to consent. A total of 60 patients were enrolled into the study.

Figure 3: Flow of Patients



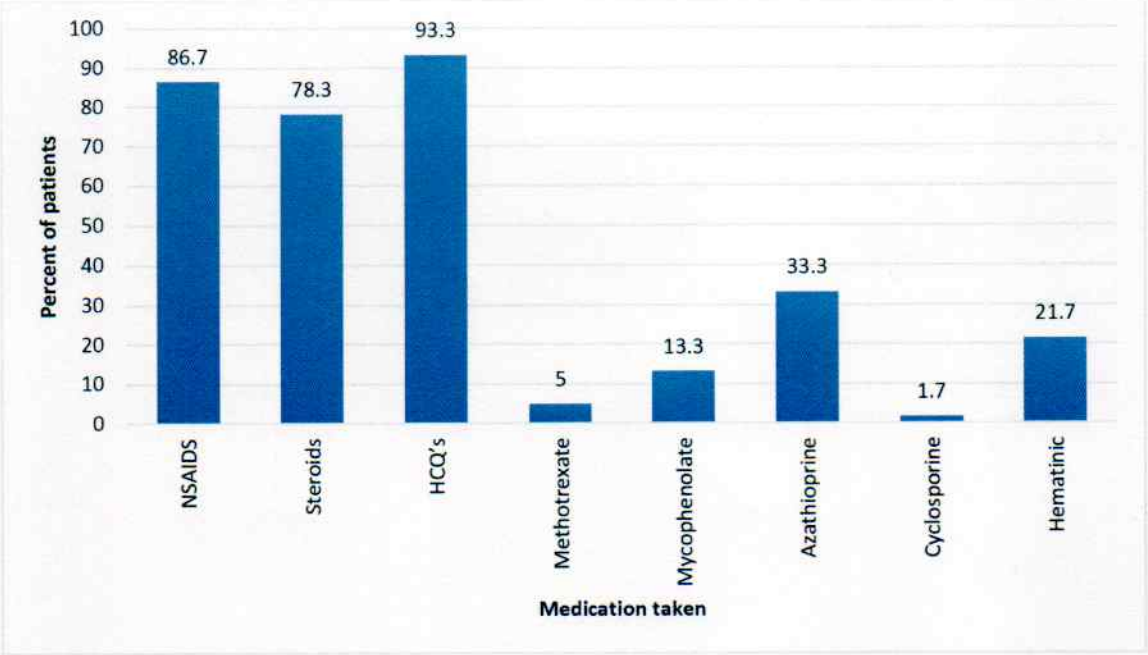
4.3 Disease history and medication

All the 60-respondent provided information on disease history and drug prescriptions for their condition. The information given was corroborated with the patient's hospital records. The mean disease duration of the patients was 42 (SD 4.2) months, with the shortest follow up being 1 month and the longest 20 years. The median duration of the disease duration was 2.0 (IQR 1.1 – 4.0) years.

The most frequently prescribed drugs were hydroxychloroquine 56 (93.3%), NSAIDs for symptomatic pain relief (86.7%), and steroids (78.3%). There was low usage of immunosuppressant drugs. There was no patient on biologic disease-modifying anti-rheumatic drugs (DMARDs).

Table 4: Duration of Illness and medication used by patients

Variable	Frequency, *n=60*	Percent
Duration of illness		
<1 year	10	16.7
1-5 years	41	68.3
>5 years	9	15.0
Medication taken		
NSAIDS	52	86.7
Steroids	47	78.3
HCQ's	56	93.3
Methotrexate	3	5.0
Mycophenolate	8	13.3
Azathioprine	20	33.3
Cyclosporine	1	1.7
Hematinic	13	21.7



4.4 Prevalence of fibromyalgia in SLE patients with chronic musculoskeletal pain

Out of the 60 studied patients, 39 patients satisfied the 2010 ACR criteria for fibromyalgia, thus we found the prevalence of 65% (95% CI 52.4% - 75.8%).

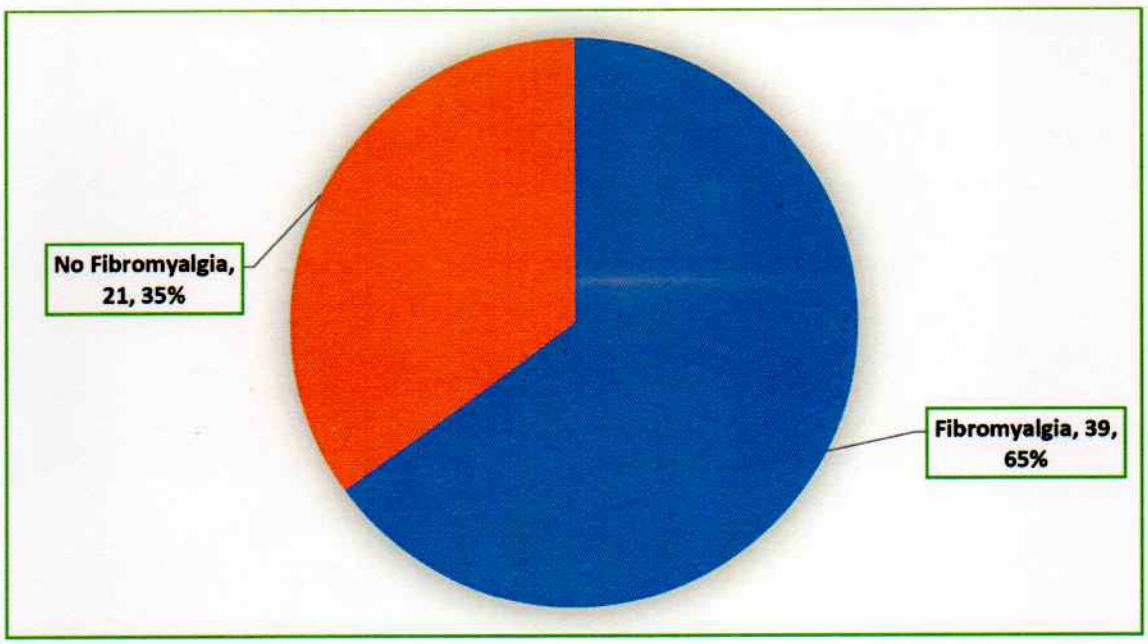


Figure 4: Prevalence of Fibromyalgia in SLE patients

4.5 Severity of Fibromyalgia Syndrome

The 39 patients were assessed for the severity of their fibromyalgia using the fibromyalgia impact questionnaire (FIQR). To assess the severity, The FIQR was rated as follows:

a. Mild 0-42
b. Moderate 43-59
c. Severe 60-74
d. Very severe 75-100

The mean FIQR score for the 39 patients with fibromyalgia was 56.3 (SD 20.4), this denotes them as having a moderate disease. Among 39 study subjects with fibromyalgia, 12 (30.8%) had mild symptoms, 5 (12.8%) had moderate symptoms, 16 (41.0%) had severe symptoms, and 6 (15.4%) had very severe symptoms.

Table 5: Severity of fibromyalgia syndrome

Severity	**Frequency**, *n=39*
Mild (0-42)	12 (30.8%)
Moderate (43-59)	5 (12.8%)
Severe (60-74)	16 (41.0%)
Very severe (75-100)	6 (15.4%)

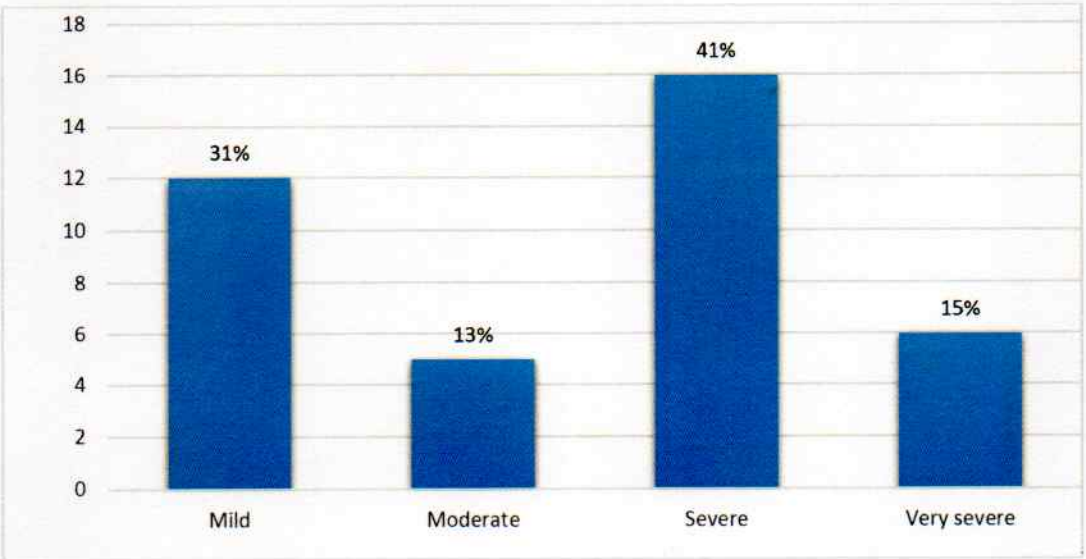


Figure 5: Percentage distribution of the patients with fibromyalgia according to the severity in the study subjects

The Pain, fatigue and unrefreshed sleep were the most frequent symptoms, while the least reported symptoms were balanced problem, memory problem and increased sensitivity to environmental stimuli (loud noises, bright light, odors or cold). All the patients with fibromyalgia reported having pain in the previous 7 days. 62% of the patients had pain score of above 7 on the pain scale, 67% of the patients scored more than 7 on the fatigue score and 62% reported a high unrefreshing sleep score of more than 7. There was equally high depressions score in fibromyalgia patients.

Table 6: Frequency of Fibromyalgia Symptoms assessed by the FIQR

Symptom category	Percentage of patients
Pain	100.0
Fatigue	100.0
Stiffness	87.2
Unrefreshing sleep	100.0
Depression	89.7
Memory	71.8
Anxiety	97.4
Tenderness to touch	92.3
Balance problems	76.9
Increased sensitivity to environment stimuli	79.5

Table 7: Frequency of Fibromyalgia Symptoms (FIQR severity score scores)

Symptom category	None	1 – 3	4 - 6	7-10
	N (%)	N (%)	N (%)	N (%)
Pain	0 (0.0)	5 (12.8)	10 (25.6)	24 (61.5)
Fatigue	0 (0.0)	2 (5.1)	11 (28.2)	26 (66.7)
Stiffness	5 (12.8)	7 (17.9)	14 (35.9)	13 (33.3)
Unrefreshing sleep	0 (0.0)	1 (2.6)	14 (35.9)	24 (61.5)
Depression	4 (10.3)	9 (23.1)	11 (28.2)	15 (38.5)
Memory	11 (28.2)	7 (17.9)	15 (38.5)	6 (15.4)
Anxiety	1 (2.6)	11 (28.2)	20 (51.3)	7 (17.9)
Tenderness to touch	3 (7.7)	7 (17.9)	17 (43.6)	12 (30.8)
Balance problems	9 (23.1)	6 (15.4)	17 (43.6)	7 (17.9)
Increased sensitivity	8 (20.5)	5 (12.8)	4 (10.3)	22 (56.4)

4.6 Quality of life in SLE patients with chronic musculoskeletal pain

The quality of life of all patients recruited was assessed using a self-administered SF-36 questionnaire, a widely validated tool for measuring health-related quality of life. It consists of 36 questions, grouped into 8 main domains with each subscale i.e. physical capability, physical role, pain, general well-being, energy levels, social well-being, emotional role, and psychological well-being. The weighted sums of the 8 scaled tallies are directly converted to 0-100 with 0 being the lowest score and 100 being the maximum score per scale. A lower score is a predictor of more disability. A total score of more or less than 50 represents a better or worse QoL respectively.

Among the 39 study subjects with fibromyalgia, 38 patients had poor quality of life, with all the aspects of QoL being impaired. The mostly affected domains by fibromyalgia were emotional well-being and physical health, where there was a significant limitation to work role and performing daily activities.

Table 8: Quality of life in patients with Fibromyalgia

Score	Frequency, *n=39*	Percent
Poor	38	97.4
Good	1	2.6

Table 9: Average Quality of life

Domains	Mean ± SD
Physical function	30.6 ±19.2
Physical health	**3.2 ±8.5**
Emotional problems	**15.4 ±36.6**
Energy / Fatigue	32.1 ±12.5
Social function	39.5 ±16.3
Emotional Well-being	39.4 ±18.0
Social functioning	37.7 ±16.2
Pain	39.7 ±12.7
General health	30.6 ±19.2

4.7 Disease Activity in SLE patients with Fibromyalgia

Disease activity was assessed using SLEDAI-2K, a validated disease activity index that assesses 24 clinical and laboratory variables, grouped into 9 domains corresponding to different organ system (central nervous system, vascular, renal, musculoskeletal, serosal, dermal, immunologic, constitutional and hematological). The disease manifestations are weighted with values ranging from 1 to 8 and then summed to give a global score ranging from 0 to 105, with the higher values correlate to the higher disease activity. The scores were further divided into 3 categories: mild disease activity (0-5), moderate disease activity (6-12) and severe disease activity (>13). There were no patients presenting with seizures, psychosis, cranial nerve disorder, cerebrovascular accident or pericarditis at the time of assessment. Complements and DNA levels were not done for majority of patients. There were two patients with visual disturbance and was related to HCQ toxicity. The median disease activity score was 7.0 (IQR 4.0-10.0). Half of the patients in the study had moderate-severe disease activity.

Table 10: Disease activity in patients with Fibromyalgia

Disease activity score	Frequency, *n=39*	Percent
Mild (0-5)	19	48.7
Moderate (6-12)	12	30.8
Severe (>13)	8	20.5

4.8 Sociodemographic and Clinical Characteristics of SLE Patients with and without Fibromyalgia

There was no statistical significance between the sociodemographic and clinical characteristics of the study subject with and without fibromyalgia except for the medical therapy. Those with fibromyalgia are more likely to be on steroids compared to those without fibromyalgia, this was statistically significant (P value= 0.023). Univariate comparisons of the sociodemographic and clinical characteristics of study participants with and without fibromyalgia are illustrated in the table below.

Table 11: Association between Demographic Characteristics and FMS

	FMS (n=39)	No FMS (n=21)	OR (95% CI)	p-value
Age, *Mean (SD)*	34.4 (8.2)	32.1 (6.4)		0.232
Age, *n (%)*				
< 20	1 (2.6)	1 (4.8)	Reference	
20 – 29	10 (25.6)	5 (23.8)	2.0 (0.1 – 39.1)	0.648
30 – 39	21 (53.8)	12 (57.1)	1.8 (0.1 – 30.6)	0.701
40 – 49	4 (10.3)	3 (14.3)	1.3 (0.1 – 31.1)	0.858
>50	3 (7.7)	0 (0)	-	
Marital Status, *n (%)*				
Married	21 (53.8)	13 (61.9)	0.6 (0.2 – 1.9)	0.413
Single	18 (46.2)	7 (33.3)	Reference	
Divorced	0 (0)	1 (4.8)	-	
Educational Level, *n(%)*				
Primary	5 (12.8)	1 (4.8)	Reference	
Secondary	14 (35.9)	15 (71.4)	0.2 (0.02 – 1.8)	0.147
University	20 (51.3)	5 (23.8)	0.8 (0.1 – 8.5)	0.853
Daily activities, *n (%)*				
Manual	10 (25.6)	3 (14.3)	Reference	
Non-manual	29 (74.4)	18 (85.7)	0.5 (0.1 – 2.0)	0.315
Occupation, *n (%)*				
Employed	20 (51.3)	6 (28.6)	Reference	
Unemployed	19 (48.7)	15 (71.4)	0.4 (0.1 – 1.2)	0.095
Duration of illness,*n(%)*				
<1	7 (17.9)	3 (14.3)	Reference	
1-5	24 (61.5)	17 (81)	0.6 (0.1 – 2.7)	0.508
>5	8 (20.5)	1 (4.8)	3.4 (0.3 – 40.9)	0.330

Drugs:				
NSAIDS				
Yes	33 (84.6)	19 (90.5)	0.6 (0.1 – 3.2)	0.524
No	6 (15.4)	2 (9.5)		
Steroids				
Yes	34 (87.2)	13 (61.9)	4.2 (1.2 – 15.2)	**0.023**
No	5 (12.8)	8 (38.1)		
HCQs				
Yes	36 (92.3)	20 (95.2)	0.6 (0.1 – 6.2)	0.664
No	3 (7.7)	1 (4.8)		
Methotrexate				
Yes	2 (5.1)	1 (4.8)	1.1 (0.1 – 12.7)	0.950
No	37 (94.9)	20 (95.2)		
Mycophenolate				
Yes	6 (15.4)	2 (9.5)	1.7 (0.3 – 9.4)	0.524
No	33 (84.6)	19 (90.5)		
Azathioprine				
Yes	16 (41.0)	4 (19.0)	3.0 (0.8 – 10.4)	0.085
No	23 (59.0)	17 (81.0)		
Hematinic				
Yes	8 (20.5)	5 (23.8)	0.8 (0.2 – 2.9)	0.767
No	31 (79.5)	16 (76.2)		

5.0 Chapter Five: Discussion

This study was aimed at finding out the prevalence and impact of fibromyalgia in SLE patients with chronic musculoskeletal pain. The study was carried out at the rheumatology clinic at the Kenyatta National Hospital (KNH), where a total of 60 SLE patients with chronic musculoskeletal pain were screened for fibromyalgia.

In our study, the majority of the respondent were female with a mean age of 34 years (IQR 29.0-38.0), in concordance with most literature that reported lupus to be a disease of female preponderance and affecting young adults (80-82). However, several comparative studies have shown that the peak age of onset is usually lower in black women (83).

In this study, a greater proportion of patients in the fibromyalgia group were noted to be on steroids. This can be explained by the fact that the overlapping symptoms of lupus and fibromyalgia can lead to misinterpretation of lupus activity, resulting in higher prescriptions of steroids. Fibromyalgia tends to increase the risk of overtreatment and misinterpretation of symptoms of lupus (84). The question that might be raised by this is whether the muscle and soft tissue pain were attributed to steroid myopathy? in the study all lupus patients classified as fibromyalgia-positive reported generalized pain of muscle and soft tissue, but none showed muscle weakness during an examination or reported an event. This observation argues against steroid myopathy as a cause of pain in fibromyalgia. Other factors like marital status, age, and occupation were found not to be statistically significant ($P > 0.05$). In other studies, SLE patients with fibromyalgia were less likely to be employed and more likely to be divorced/separated, an observation that was not elucidated by our study (14).

In our study, the prevalence of fibromyalgia in SLE patients was 65%, higher than in previous studies which ranged between 22-61%. This verifies that fibromyalgia is indeed common in this group of patients. In a cross-sectional study of 102 patients with SLE in the USA, the 1990 ACR criteria were used to diagnose fibromyalgia and a prevalence of 22% was reported (14). In another descriptive study in Brazil, Luiza et al reported a 12% prevalence of fibromyalgia among 60 patients with lupus, they used similar tools as in our study; the 2010 ACR criteria to diagnose fibromyalgia, and FIQR to evaluate the functional capacity and health status of their patients. Disease activity and quality of life were assessed using SLEDAI and SF-36 respectively (18).

A higher prevalence of fibromyalgia at 40% was reported in a comparable study in Israel among 75 patients with SLE (71). In India, a low prevalence of fibromyalgia was reported at 8.2% among 158 patients with lupus. The authors hypothesized that a strong family support system, the virtual lack of disability benefits, and/or racial variations in pain threshold could be the likely factors responsible for the low prevalence of fibromyalgia observed in this population (73).

In a case-control report in Iraq, a hundred patients with SLE and healthy controls were evaluated for fibromyalgia, the 1990 ACR criteria for fibromyalgia were applied to both groups and lupus activity was measured using the SLEDAI. The prevalence of fibromyalgia was reported to be 26% in the SLE group compared to 2% in the controls (85). In another study, the prevalence of FM in SLE was reported to be as high as 61% (86).

These differences could be a result of geographical influences, sociocultural differences, therapeutic factors, and racial variation in the threshold of pain. We recognize the large variation in the prevalence rates compared to other studies and ascribed this to an ethnic difference in this study population (largely black African), low socioeconomic status, and lack of medical disability benefits. These findings corroborate a study done by Edward et al in evaluating the differences in pain tolerance in different ethnic groups, they noted that African-American subjects reported higher levels of clinical pain as well as greater pain-related disability than whites (87). Moreover, racial difference was again reported by Gansky et al in the US, where there was a higher prevalence of fibromyalgia syndrome in black Americans than the whites, and this was attributed to poor socioeconomic status (28). All the papers that studied the association of fibromyalgia with socioeconomic status reported in consensus that the lower the household income, the higher the prevalence rate of fibromyalgia.

In the study, most of the patients had severe diseases. Pain, lack of energy, and poor sleep were the most common symptoms of fibromyalgia. The higher pain score in fibromyalgia is a predictable finding because these patients have increased central pain processing and low endogenous pain inhibition. Deprived sleep is common in fibromyalgia syndrome and usually, results in increased daytime fatigue, as results Patients with fibromyalgia have difficulty in performing daily living activities and achieving their goals.

A high FIQR mean score of 56.3 was reported, reflecting that most of our patients had moderate disease, in comparison to the previous local studies on fibromyalgia in HIV and diabetics patients (25,26), the average mean score of 56.3 is higher than in HIV (50.1) and diabetics (51.9). This might be explained by the fact that patients with fibromyalgia in diabetes and HIV undergo counseling sessions at each visit to their respective clinics. The counseling involves psychotherapy and CBT, which help them cope with pain.

More than half of the patients with fibromyalgia had active disease, with a median disease score was 7.0 (IQR 4.0-10.0). Contrary to what was seen in other studies where fibromyalgia causes slight or no impact on the activity of lupus, the extensive disease activity seen in this population can be attributed to multiple factors including early onset of the disease and long disease duration of the study subjects (from 1 month to 20 years), as well as high cost of treatment (we are not optimizing the treatment of lupus, especially the use of biologics) and irregular follow-ups.

Concerning the quality of life as measured by SF-36 in our study, it can be seen that fibromyalgia was associated with poor QoL in patients with lupus. All 8 domains in assessing QoL were negatively impaired, with emotional well-being and physical health being the most affected aspect by fibromyalgia, limiting their daily activity and ability to work. These findings correspond to the literature that fibromyalgia has a significant negative impact on the QoL, working ability and efficacy in patients living with lupus (14,72). A comparable study by Luiza et al verify these findings. They reported a strong impact of fibromyalgia on the QoL in patients with SLE, with great intensity of symptoms. The most affected domain by fibromyalgia in the Brazilian population were pain, physical aspects and emotion resulting to incapacity for daily activities (18). Another study in Israel reported that fibromyalgia had adversely affected the QoL and ability of SLE patients to cope. In the study, the patients were dissatisfied with their QoL, especially the general health aspect (69). In a Canadian study by Gladman et al, it was reported that the presence of fibromyalgia had a strong correlation with the 8 domains of SF-36 and is a major contributor to poor QoL in patients with lupus (15).

Our study reiterates the fact that fibromyalgia is not only prevalent in patients with lupus but has a negative impact on the quality of life of these patients, thus early recognition of fibromyalgia is relevant to every physician who manages patients with lupus.

Conclusion

Fibromyalgia is a major problem in SLE patients with chronic musculoskeletal pain with a prevalence rate of 65%. It is most predominant in middle-aged females and a well-educated population. Fibromyalgia patients are more likely to be on steroids. High-intensity of fibromyalgia symptoms was seen in patients with lupus. The presence of fibromyalgia poorly impacts the QoL of patients with lupus, causing incapacity for daily living by significantly affecting emotional well-being and physical health functioning.

Study Strengths

1. New data to guide future research- First study to look at both the prevalence and impact of fibromyalgia in patients with SLE in Kenya and Africa at large.

Study Limitations

a) Recall biased as patients were meant to answer questions that had occurred over the last seven days.

b) Single center study- largely enrolling patients from urban and suburban habitations, patients from the community levels may have been missed.

Recommendation

- Screening for Fibromyalgia as standard care among SLE patients with chronic musculoskeletal pain for early therapy and preventing overtreatment.
- Quality of life should be assessed for all SLE patients presenting with musculoskeletal pain using SF-36.
- Regular counseling and psychosocial support to patients with fibromyalgia in the rheumatology clinic to enable them to cope with pain.
- The need for a larger, multicenter population-based study that can assess both patients in primary and secondary health care facilities.

Study Budget

Item	Quantity	Unit Cost (Ksh)	Total
Training and renumeration	2 personnel	15,000	30,000
Stationery and Printing	Data collection forms, research booklets	20,000	20,000
Statistician Allowance	1	30,000	30,000
Laboratory expenses	TBC, CK, Urinalysis	150,000	150,000
Ethic committee review fee		2000	2000
Contingency		30,000	30,000
Total (Ksh)			**262,000**

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Appendices

Appendix 1: Informed Consent Form

Patient Study No: _____

1. Introduction

My name is Dr. Said Awadh Salim, a post-graduate student at the University of Nairobi. I am undertaking a study to determine the prevalence and impact of fibromyalgia on quality of life and disease activity in SLE patients on follow-up at the Kenyatta National Hospital.

2. Type of Research Intervention

Should you agree to participate in the study, you will:

i. Sign a consent form and participate in a survey.
ii. Answer questions about your personal bio-data i.e. age, gender, marital status, level of education. Information regarding your disease will be obtained and verified from your medical records. Your response will be noted and filled into the study questionnaire.
iii. Be asked if you experience any pain in the body and presence of any associated symptoms (like fatigue, sleep disturbances) and how the disease affects your life and activities of daily living (ADL). Physical examination will be performed to establish the diagnosis.
iv. Undergo venipuncture for withdrawal of about 4 mls of blood for tests. These tests will enable me determine your total blood count and creatinine phosphokinase. You will also provide a urine sample for urinalysis.
v. Be referred to a consultant rheumatologist to confirm the diagnosis and followed up for further management.

3. Participation in this study

i. Is voluntary.
ii. You are free to terminate the interview and withdraw from the study at any time.
iii. You will not be victimized if you refuse to participate in the study.
iv. You are free to ask any question before enrollment or at any given time during the study.
v. All the information collected will remain confidential.

4. Purpose of study

We want to find the prevalence and association of fibromyalgia in SLE patients on follow-up at the KNH. This study will help us manage chronic musculoskeletal pain better in SLE patients and also to recommend for better control of the pain symptoms. The results will be published in a medical journal and used for academic purposes.

5. Duration

The study will take place over a 3 months period at the rheumatology clinic. Each participant will be enrolled once.

6. Participants Risks

Minor discomfort or swelling at the injection site during collection of blood sample.

7. Participants Benefit

Free evaluation of your total blood count and urinalysis, free copy of your results will be availed to you on request. The findings of this study will assist in providing better care for you and other SLE patients.

8. Participants Declaration

As an indication that you have agreed to participate in this study, kindly sign below;

I, ... do hereby consent to participate in this study carried out by Dr. Said Awadh Salim, the nature of which has been explained to me. I have understood the purpose of this study and my questions have been answered in the language that I understand.

Participant signature: .....

Researchers signature: .....

Date: ...../...../.....

Whom to contact:

If you have any queries during the study, you may contact the following:

Dr. Said Awadh Salim- 0705554846

Prof. Omondi Oyoo- 020-27254552

Dr. Eugene Genga -0723596189

Appendix 2: Informed Consent Form (Swahili version)

Patient Study No: _____

Kuhusu Idhini

Kwa majina ni Dr. Said Awadh Salim, mwanafunzi katika chuo kikuu cha Nairobi. Ninafanya utafiti kuhusu ugonjwa unaoathiri misuli, mifupa na viungo kwa wenye ugonjwa wa chavi cha uso (SLE).

Lengo la utafiti

Utafiti huu utatuwezesha kujua idadi ya watu ambao wameathirika na ugonjwa huo kwa walio na ugonjwa wa chavi cha uso (SLE) na jinsi tutaweza kuwasaidia kimatibabu.

Faida ya kushiriki katika uchunguzi

Utafitii huu utasaidia pakubwa kuelezea matabibu uwepo wa ugonjwa huu na jinsi ya kuukabili kwa walio na ugonjwa wa chavi cha uso (SLE). Mapendekezo ya utafiti huu utasaidia kuboresha huduma wanazozipata wagonjwa hawa hususan wenye uchungu au maumivu makali katika viungo mbali mbali.

Mbali na hayo, uchunguzi wote utafanywa bure bilashi. Mpelelezi mkuu atagharamia malipo yote. Isitoshe, matokeo ya utafiti huu yatachapishwa katika jarida la kimataifa na kutumiwa na wanafunzi wa udaktari.

Madhara ya kushiriki

Kwa kushiriki katika utafiti huu, mshiriki hatapata madhara yoyote ila ni maumivu madogo tu wakati wa kutolewa kipimo cha damu.

Idhini ya kuhusika

Kuhusika kwako katika utafiti huu ni kwa hiari, uko huru kutoendelea wakati wowote wa utafiti bila ya ubaguzi wa aina yoyote.

Sahihi ya mhusika: ..... Tarehe: .....

Sahihi ya mtafiti: ..... Tarehe: .....

Mawasiliano:

Kwa maswali au mapendekezo yoyote, tafadhali wasiliana na nambari zifuatazo:

Dr. Said Awadh Salim- 0705554846

Prof. Omondi Oyoo- 020-27254552

Dr. Eugene Ngenga- 0723596189

Appendix 3: Assent form (<18 years)

Patient Study No. _____

As an indication that you have agreed to participate in this study, kindly sign below;

I, ... do hereby consent to participate in this study carried out by Dr. Said Awadh Salim, the nature of which has been explained to me. I have understood the purpose of this study and my questions have been answered in the language that I understand.

Patients signature: .....

Parent/Guardian signature: ..... Date: .....

Researchers signature: ..... Date: .....

Appendix 4: Assent Form (<18 years) Swahili Version

Patient Study No. _____

Kuhusika kwako katika utafiti huu ni kwa hiari, uko huru kutoendelea wakati wowote wa utafiti bila ya ubaguzi wa aina yoyote.

Sahihi ya mhusika: ..... Tarehe: .....

Sahihi ya Mzazi/Mlezi: ..... Tarehe: .....

Sahihi ya mtafiti: ..... Tarehe: .....

Appendix 5: Investigator's statement

I, the investigator has fully educated the research participant on the intention and implications of this study.

Signed: ..... . Date: .....

Appendix 6: Screening Questionnaire

Participant study number: _____ Hospital No: _____

Study Date: _____

1. Consent / Assent Given: Yes [ ] No [ ] If yes proceed to 2

2. Age above 15 years: Yes [ ] No [ ] If yes proceed to 3

3. For official use only

Recruited? Yes [ ] No [ ]

Interviewers Name: _____

Signature: ..... Date: _____

Appendix 7: Study Proforma

Study No: _____ **Study Date:** _____

1. **Socio-demographic Data**

   Sex: M [ ] F [ ]

   Age: [ ] years [ ] Months

   Marital status: Married [ ] single [ ] Divorced [ ] Widowed [ ]

   Occupation: [ ] 1 = Employed 2 = Unemployed 3 = Retired 4 = others

   Daily activities: [ ] 1 = Manual labor 2 = Non-manual labor

   Education Level: [ ] 1= primary 2= secondary 3= university/college 4= others

2. **Clinical Data**

   a) Duration of the Disease from the onset of diagnosis: [ ] yrs [ ] Months

   b) Have you been on treatment with these drugs?

Drug	Yes (√) / No (×)	Duration	Current Dose
NSAIDs			
Steroids			
HCQs			
Methotrexate			
Leflunomide			
Mycophenolate			
Azathioprine			
Cyclosporine			
Hematinic			

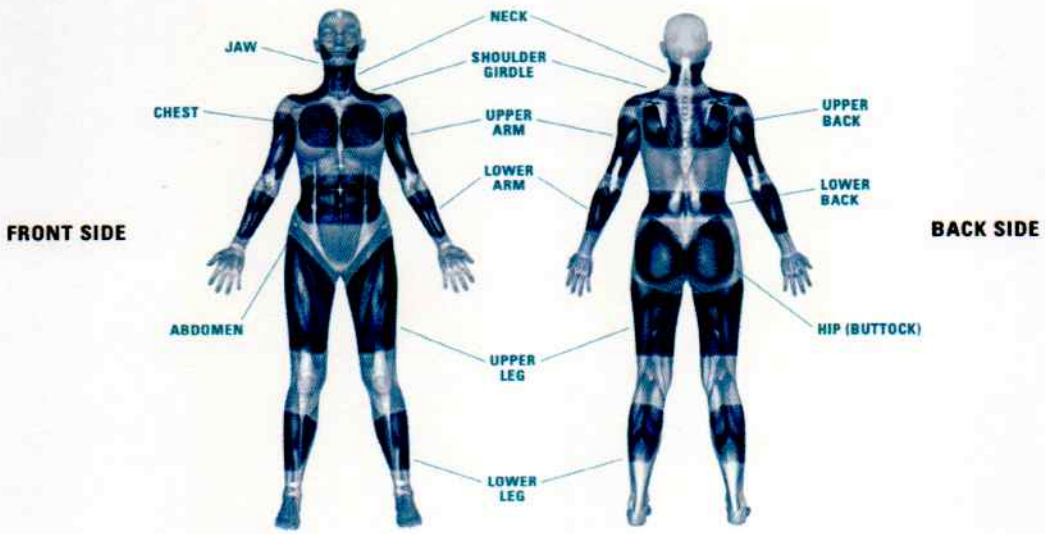
c) Presence of Musculoskeletal pain? Yes [ ] No [ ]

d) If yes, duration of symptoms?

< 3 months [ ] >3 months [ ]

e) Please indicate if you had pain or tenderness in each of the following areas over the past 7 days?

Right side	**Yes √**	**No ×**	**Trunk**	**Yes √**	**No ×**	**Left side**	**Yes √**	**No ×**
Jaw			Neck			Jaw		
Shoulder			Upper back			Shoulder		
Upper Arm			Chest/Breast			Upper Arm		
Lower Arm			Abdomen			Lower Arm		
Hip/Buttock			Low back			Hip/Button		
Upper Leg						Upper Leg		
Lower leg			**WPI Score**	**(0-19)**	**=___**	Lower Leg		



f) Part 2A: Symptom Severity Scale (SSS)

For the each of the 3 symptoms below, indicate the level of severity over the past week using the following scale:

	Fatigue	**Waking unrefreshed**	**Cognitive symptoms**
0 = no problem			
1 = slight or mild problems, generally mild or intermittent			
2 = moderate, considerable problems, often present and/or at a moderate level			
3 = severe, pervasive, continuous, life-disturbing problems			

Total the scale numbers for all the 3 categories and write the number here: ☐

g) Part 2B: Other Somatic symptoms

How many of the following has the patient had in the past 6 months?

Symptoms	**Yes (1)**	**No (0)**
Pain or cramps in lower abdomen		
Depression		
Headache		

Add the scores from parts 2a and 2b (The SS Score, can range from 0 to 12).

Write the patient's SS score here: ☐

h) Satisfy criteria for Fibromyalgia?

- WPI ≥7 and SS scale score ≥5

OR

- WPI 3 - 6 and SS scale score ≥9

Appendix 8: Revised Fibromyalgia Impact Questionnaire (FIQR)

Patients Study No: _____

Domain 1 Directions: For each of the following 9 questions, place an X in the box that best indicates how much your fibromyalgia made it difficult to do each of the following activities over the past 7 days

Brush or comb your hair	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult
Walk continuously for 20 minutes	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult
Prepare a homemade meal	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult
Vacuum, scrub or sweep floors	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult
Lift and carry a bag full of groceries	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult
Climb one flight of stairs	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult
Change bed sheets	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult
Sit in a chair for 45 minutes	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult
Go shopping for groceries	No difficulty ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Very difficult

Function subtotal: ☐

Domain 2 Directions: For each of the following 2 questions, check the one box that best describes the overall impact of your fibromyalgia over the last 7 days.

Fibromyalgia prevented me from accomplishing goals for the week	Never ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Always
I was completely overwhelmed by my fibromyalgia symptoms	Never ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Always

Overall Impact sub-total: ☐

Domain 3 directions: For each of the following 10 questions, select the one box that best indicates the intensity of your fibromyalgia symptoms over the past 7 days:

Please rate your level of pain	No pain	Unbearable pain
Please rate your level of energy	Lots of energy	No energy
Please rate your level of stiffness	No stiffness	Severe stiffness
Please rate the quality of your sleep	Awoke rested	Awoke very tired
Please rate your level of depression	No depression	Very depressed
Please rate your level of memory problems	Good memory	Very poor memory
Please rate your level of anxiety	Not anxious	Very anxious
Please rate your level of tenderness to touch	No tenderness	Very tender
Please rate your level of balance problems	No imbalance	Severe imbalance
Please rate your level of sensitivity to loud noises, bright lights, odors and cold	No sensitivity	Extreme sensitivity

Symptom Sub-total: ☐

FIQR total score: ☐

Scoring System of FIQR and SIQR

Each of the three domains (function, overall impact and symptoms) are scored on a scale of 0 to 10. The 11 boxes represent the numbers 0 to 10 from left to right.

Step 1: Sum the scores for each of the three domains

Step 2: Divide domain 1 score by 3

Divide domain 2 score by 1

Divide domain 3 score by 2

Step 3: Add the three resulting domain scores above to obtain the total score of FIQR and SIQR (ranging from 0-100)

Appendix 9: SLEDAI-2K

Weight	Present	Descriptor	Definition
8		Seizure	Recent onset, exclude metabolic, infectious or drug causes
8		Psychosis	Altered ability to function in normal activity due to disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Exclude uremia and drug causes
8		Organic Brain Syndrome	Altered mental function with impaired orientation, memory, or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious or drug causes.
8		Visual disturbance	Retinal changes of SLE. Include cytoid bodies, retinal hemorrhages, serous exudates or hemorrhages in the choroid, or optic neuritis. Exclude hypertension, infection or drug cause
8		Cranial nerve disorder	New onset of sensory or motor neuropathy involving cranial nerves
8		Lupus headache	Severe, persistent headache: may be migranious but must be non-responsive to narcotic analgesia
8		CVA	New onset cerebrovascular accident(s). Exclude arteriosclerosis
8		Vasculitis	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, or biopsy or angiogram proof of vasculitis
4		Arthritis	> 2 joints with pain and signs of inflammation (i.e. tenderness, swelling or effusion).
4		Myositis	Proximal muscle aching/weakness, associated with elevated creatinine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis
4		Urinary cast	Heme-granular or red cell casts
4		Hematuria	> 5 red blood cells/ high power field. Exclude stone or other cause
4		Proteinuria	> 0.5 g /24 hr
4		Pyuria	> 5 white blood cells / high power field. Exclude infection.
2		Alopecia	Abnormal, patchy or diffuse loss of hair

2		Mucosal ulcers	Oral or nasal ulcerations
2		Pleurisy	Pleuritic chest pain with pleural rub or effusion. Or pleural thickening
2		Pericarditis	Pericardial pain with at least one of the following: rub, effusion, electrocardiographic confirmation or echocardiographic confirmation
2		Low compliment	Decrease in CH50, C3 OR C4 below lower limit of normal for testing laboratory
2		Increased DNA binding	Increased DNA binding by Farr assay above the normal range for testing laboratory
1		Fever	$> 38^0$C. Exclude infectious cause.
1		Thrombocytopenia	< 100000 platelets/x 10^9, exclude drug causes
1		Leukopenia	< 3000 white blood cells/x 10^9, exclude drug causes
Total Score (Sum of weights marked present) =			

Appendix 10: SF-36 Questionnaire

Patients Study No: _____

For each of the following questions, choose one best answer:

1. In general, would you say your health is:
    - o 1- Excellent
    - o 2- Very good
    - o 3- Good
    - o 4- Fair
    - o 5- Poor
2. Compared to one year ago, how would you rate your health in general now?
    - o 1- Much better now than one year ago
    - o 2- Somewhat better now than one year ago
    - o 3- About the same
    - o 4- somewhat worse now than one year ago
    - o 5- Much worse now than one year ago

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot (0)	Yes, limited a little (2)	No, not limited at all (3)
3. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports			
4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf			
5. Lifting or carrying groceries			
6. Climbing several flights of stairs			
7. Climbing one flight of stairs			
8. Bending, kneeling, or stooping			
9. Walking more than a mile			
10. Walking several blocks			
11. Walking one block			
12. Bathing or dressing yourself			

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	Yes	No
13. Cut down the amount of time you spent on work or other activities	o 1	o 2
14. Accomplished less than you would like	o 1	o 2
15. Were limited in the kind of work or other activities	o 1	o 2
16. Had difficulty performing the work or other activities (for example, it took extra effort)	o 1	o 2

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	Yes	No
17. Cut down the amount of time you spent on work or other activities	o 1	o 2
18. Accomplished less than you would like	o 1	o 2
19. Didn't do work or other activities as carefully as usual	o 1	o 2

20. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?
    - o 1- Not at all
    - o 2- Slightly
    - o 3- Moderately
    - o 4- Quite a bit
    - o 5- Extremely
21. How much bodily pain have you had during the past 4 weeks?
    - o 1- None
    - o 2- Very mild
    - o 3- Mild
    - o 4- Moderately
    - o 5- severe
    - o 6- very severe
22. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
    - o 1- Not at all
    - o 2- A little bit
    - o 3- Moderately
    - o 4- Quite a bit
    - o 5- Extremely

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks:

	All of the time (1)	**Most of the time (2)**	**A good bit of the time (3)**	**Some of the time (4)**	**A little of the time (5)**	**None of the time (6)**
23. Did u feel full of pep?						
24. Have you been a very nervous person?						
25. Have you felt so down in the dumps that nothing could cheer you up?						
26. Have you felt calm and peaceful?						
27. Did you have a lot of energy?						
28. Have you felt downhearted and blue?						
29. Did you feel worn out?						
30. Have you been a happy person?						
31. Did you feel tired?						

32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?
    - o 1- All of the time
    - o 2- Most of the time
    - o 3- Some of the time
    - o 4- A little of the time
    - o 5- None of the time

How TRUE or FALSE is each of the following statements for you.

	Definitely True (1)	**Mostly True (2)**	**Don't know (3)**	**Mostly False (4)**	**Definitely False (5)**
33. I seem to get sick a little easier than other people					
34. I am as healthy as anybody I know					
35. I expect my health to get worse					
36. My health is excellent					

Step 1: Recording items

Item numbers	Change original response category	To recoded value of:
1, 2, 20, 22, 34, 36	1 → 2 → 3 → 4 → 5 →	100 75 50 25 0
3, 4, 5, 6, 7, 8, 9, 10, 11, 12	1 → 2 → 3 →	0 50 100
13, 14, 15, 16, 17, 18, 19	1 → 2 →	0 100
21, 23, 26, 27, 30	1 → 2 → 3 → 4 → 5 → 6 →	100 80 60 40 20 0
24, 25, 28, 29, 31	1 → 2 → 3 → 4 → 5 → 6 →	0 20 40 60 80 100
32, 33, 35	1 → 2 → 3 → 4 → 5 →	0 25 50 75 100

Step 2: Averaging items to form Scale

Scale	No of Items	After recording in step 1, average the following items
Physical function	10	3, 4, 5, 6, 7, 8, 9, 10, 11, 12
Role limitation due to Physical Health	4	13, 14, 15, 16
Role limitation due to emotional problems	3	17, 18, 19
Energy/ Fatigue	4	23, 27, 29, 31
Emotional well-being	5	24, 25, 26, 28, 30
Social Functioning	2	20, 32
Pain	2	21, 22
General health	5	1, 33, 34, 35,36

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