METABOLIC SYNDROME IN RHEUMATOID ARTHRITIS PATIENTS: PREVALENCE AND RISK FACTORS.

A dissertation submitted in partial fulfilment of the requirements for the Master of Medicine Degree (MMed) in Internal Medicine of the University of Nairobi.

By

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Declaration

I hereby confirm that this dissertation is my original work and has not been presented elsewhere for examination.

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Dedication

To the boys,

Beda and Mishael

The arrows in my quiver

That you may one day appreciate the product of sacrifice, going the extra mile.

&

That getting out of your comfort zone is in itself part of growth

And their mother,

Mercy

For being the pillar around which my life revolves

List of Abbreviations

ACC	American College of Cardiology
ACR	American College of rheumatology
AIDS	Acquired immunodeficiency syndrome
ASCVD	Atherosclerotic cardiovascular disease
BMI	Body mass index
BP	Blood pressure
CI	Confidence Interval
CRP	C-reactive protein
CVD	Cardiovascular disease
DAS-28	Disease activity score - 28
ESR	Erythrocyte sedimentation rate
EULAR	European League Against Rheumatism
FBS	Fasting blood sugar
HDL	High density lipoproteins
HIV	Human immunodeficiency virus
KNH-UON	Kenyatta National Hospital - University of Nairobi
Met-S	Metabolic syndrome
NSAIDS	Non-steroidal anti-inflammatory drugs
RA	Rheumatoid arthritis
RBS	Random blood sugar
ROC	Receiver operating characteristics
T2DM	Type 2 diabetes mellitus
TG	Triglycerides
TG	Triglycerides
UoN	University of Nairobi

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Abstract

Background: Rheumatoid arthritis (RA) predisposes afflicted patients to an increased risk of metabolic syndrome (Met-S) and cardiovascular disease. The prevalence of Met-S in RA has variably been reported in different populations as has been the strength of association of associated risk factors.

Broad Objective: To determine the prevalence, and associated risk factors, of Met-S among RA patients.

Study Design and Site: A descriptive cross-sectional study done at the KNH rheumatology clinic.

Participants and Methods: A total of 127 patients with established RA were recruited. The following parameters were obtained/calculated for further analysis: patients' demographics, waist circumference, CRP/ESR, BP, FLP, RBS, disease duration, disease activity, BMI and ten-year ASCVD risk. Presence of Met-S was ascertained as per guidelines.

Data Management: Analysis of the data was carried out using SPSS. Categorical data was reported as frequencies, whereas continuous data was expressed in means and standard deviation. Appraisal of patient and disease features between patients with Met-S and those without Met-S was carried out using the Independent Student's-t and Chi-square tests. Logistic regression was performed to estimate the impact of moderator variables, adjusting for age, sex and baseline characteristics. Throughout the analysis, a $p<0.05$ was considered statistically significant at a 95% CI. Ethical approval was granted by the KNH-UON Ethics and Research Committee.

Results: Of the 127 participants, 115 were female while 12 were male. The mean age was 51.48±15.7 years while age at diagnosis was 43.29±13.81 years. The median duration of RA treatment was 6.65 years. Eighty-three patients (65.4%) had a waist circumference above the set cut off while 58 (45.7%) and 16 (12.6%) were overweight and obese respectively. Sixty-eight patients (53.5%) were hypertensive, 18 (14.2%) were diabetic while 38 patients (29.9%) had dyslipidaemia. Twenty-seven patients (21.26%) met the criteria for Met-S. A majority (55.12%) of the patients had advanced disease activity. Of the 97 patients aged above 40 years,

52.58% had either intermediate or high-risk CVD scores. Univariate analysis, age at diagnosis (OR= 1.07, p<0.001), disease duration (OR= 1.08, p=0.004), disease activity (OR= 1.76, p=0.004), elevated CRP (OR= 1.01, p=0.021) and steroid use (OR= 2.90, p=0.018) were associated with Met-S.

Conclusion: Despite prevalence of METS being lower than the global average, the components of METS were highly prevalent and there was sub-optimisation of many of the modifiable risk factors.

1. Introduction and Literature Review

1.1 Introduction

Rheumatoid arthritis (RA), considered the commonest inflammatory arthritis, is an autoimmune disease of unknown cause characterised by symmetrical synovitis and joint inflammation (1). The global prevalence of RA is approximately 1% with ranges from 0.12% to as high as 6.8% amongst native Americans (2). Among Africans, RA's prevalence has been documented to range between 0.06% and 3.4% (1,3). Untreated, RA is a prominent cause of chronic indisposition and is associated with major systemic complications culminating in a reduced health-associated quality of life, diminished labour capacity, reduced life expectancy and increased cost of living among affected patients (1,4).

Patients living with RA have been reported to have an heightened risk of cardiovascular disease (CVD) (5). The predisposition to CVD in these patient is precipitated by, among other factors metabolic syndrome (Met-S), a collection of interrelated disorders that include increased blood pressure, central obesity, raised blood glucose levels and dyslipidaemia (including lowered high density lipoproteins and increased levels of triglycerides) (6,7). Globally, the prevalence of Met-S in RA patients is reported to range between 14% and 64% (8–11). Furthermore, the occurrence of Met-S in RA patients has variably been known to be determined by several factors including medication use, duration of disease and affected patient's age (10). How these factors affect the occurrence of Met-S among RA patients in our local set up has similarly not been documented. Furthermore, Met-S has variably been shown to worsen RA and predispose affected patients to high CVD risk. However, this association has hardly been investigated in our local population despite the different socio-economic environment.

The individual components of Met-S have similarly been known to occur variably among patients with RA. These include prevalence of hypertension and diabetes among RA patients (12–14) and the frequency of dyslipidaemia (8,11). The adequacy of the control of some of these easily modifiable components of Met-S has additionally been reported to be subpar in previous publications. Furthermore, the strength of association

of these factors with the severity of RA has been known to vary in previous studies. This study therefore aimed at determining the prevalence, and associated risk factors, of metabolic syndrome in patients living with RA.

1.2 Literature Review

1.2.1 Rheumatoid Arthritis: Definition and Risk Factors

Rheumatoid arthritis (RA) is an autoimmune disease of unidentified cause presenting with symmetrical synovitis and joint irritation. It largely affects small joints of the feet, hands and wrists. The disease is further characterized by the generation of self-recognizing antibodies like rheumatoid factor and anti-citrullinated protein antibodies which, together with the attendant clinical picture, form part of the RA-diagnostic criteria (1,15). Untreated, RA is a principal cause of chronic morbidity and major systemic complications culminating in a reduction in affected patients' quality of life, diminished labour capacity, reduced life expectancy and increased cost of living in affected patients (1,4).

Risk factors for the development of RA include being female, genetic predisposition - mainly involving the HLA-DR4 gene, and environmental exposures including cigarette smoking and periodontal infections (1,15–17). One's ethnicity and a western based diet have also been implicated in predisposition to RA (1). Another key disposition to developing RA is increased body mass index (BMI), especially in females, and the attendant loss in muscle mass (18,19).

1.2.2 Prevalence of Rheumatoid Arthritis

The global prevalence of RA is approximately 1% (1) and ranges from 0.12% to as high as 6.8% among native Americans. RA is similarly, highly prevalent among the indigenous people of Oceania including the indigenous people of Australia and New Zealand. The prevalence of RA however, shows distinct regional differences with highest rates reported in high income countries while Western Sub-Saharan Africa and South East Asia registering the lowest disease burden rates for RA (4). Within specific countries, the prevalence of the disease is higher among urban dwellers, considered more economically endowed, compared to the rural populations (20). The global prevalence of RA has however, been increasing since 1990 (4,21).

RA's prevalence among Africans is documented to range between 0.06% and 3.4% (3). The African ethnicity has been associated with an earlier age of disease onset, a higher percentage of affected patients being female and a more severe disease (22). Delayed specialist referral and untreated or inadequately treated disease have been blamed for the higher than the global average in the prevalence of severe RA disease activity and more functional loss among African patients (15). Other population differences noted in the epidemiology of RA in Africa is a higher median age of affected patients, and a longer duration of the disease (1,15).

Relative to the general population, persons living with RA have a greater mortality risk (23). Cardiovascular disease (CVD), of which RA patients have a two-fold greater hazard relative to the population at large (24), has been identified as the commonest cause of mortality in these patients (1,25). This risk has been associated with the enhanced rates of elevated blood pressure, dyslipidaemia, diabetes mellitus and obesity among those with RA. A high CVD risk has been described in over 50% of RA patients (25) with affected patients having higher 30-day mortality rates relative to non-RA patients following a newly diagnosed myocardial infarction or heart failure (26,27). Among the established causes of CVD in affected patients is metabolic syndrome, whose prevalence has been reported to be up to four times in RA patients with established CVD risks compared to those who do not have these risks (6,25).

1.2.3 Metabolic Syndrome: Definition

Metabolic syndrome is a known risk factor for the onset of type 2 diabetes and CVD in affected patients (5,6). Its prevalence among RA patients has been reported to be up to four times higher relative to the larger population (25). It comprises of a cluster of interrelated factors that include elevated blood pressures, central obesity, raised blood glucose levels and dyslipidaemia (including lowered high density lipoprotein and high triglycerides levels) (6,7). In 2009, a joint statement was issued that defined Met-S as the presence of abnormalities in any 3 of the 5 aforementioned parameters (5). Met-S has traditionally been linked with an increased severity of RA (8,9). This strength of association, in our local population, has however not been documented.

1.2.4 Metabolic Syndrome in Rheumatoid Arthritis

The prevalence of Met-S occurs in up to 64% (range 14% - 64%) of patients with RA (8–11). These studies were however mostly done amongst European, North American, Asian, South American and North African ethnic populations. These regions are associated with a better healthcare access compared to sub-Saharan Africa, including Kenya. For instance, Met-S in RA in patients of Asian descent was found to be significantly higher (36.5% vs. 15.5%) than in healthy controls (28). The study however had a shorter average disease duration activity of 3.33+/-1.99 years in contrast to a prospective study conducted among South American RA patients that showed that the prevalence of Met-S had increased by 15.5% (from 43.9% to 59.4%) in 8 years (29). Another study among Pakistani RA patients reported a similar prevalence of Met-S 32.7% (30). The patients were however much younger (between 16 and 40 years of age, average age of 33 years). Studies with older patients on the other hand, have recorded higher prevalence rates of Met-S in RA (29,31). Similarly, studies involving predominantly Caucasian populations have reported different prevalence rates for Met-S in RA, with age of study participants and duration of disease being among the different explanations fronted for this observation (10,32,33).

Among North Africans, Met-S' prevalence among RA patients was reported to be up to 48% while the average disease duration was 7.8 years (34). This study further reported a positive correlation of Met-S with steroid use. They however did not determine the effect of dosage nor duration of steroid use among RA patients on Met-S. Other studies have reported conflicting association of Met-S with methotrexate use with some reporting a positive association (30) while others found no association (34). The effect of longer disease duration warrants further investigation. Furthermore, the prevalence of the various components of Met-S has been documented to be considerably higher compared to the overall prevalence of Met-S in RA (28,30,34).

1.2.5 Adiposity in Rheumatoid Arthritis

Increased abdominal adiposity and body mass index (BMI) have been correlated with Met-S in affected persons. For instance, waist circumference which is used as a marker of abdominal adiposity (35), has been

shown to be much higher among RA patients with severe disease activity (11). Waist circumference, however, has been shown to vary with one's ethnicity (5,7) and thus ethnic specific diagnostic cut-offs have been established with most recent cut-offs for the Kenyan population being 94cm and 86cm for men and women respectively (7). The association of waist circumference, as a marker of Met-S, with disease severity in persons living with RA in our setting has however, not been established.

Another measure of habitus adiposity, is body mass index (BMI) (36). It ranges from 18 to 25 for healthy sub-Saharan natives. Patients with RA and an elevated BMI have been reported to have an increased prevalence of Met-S (8). Hardly any studies however, have documented the link of BMI and disease severity among Kenyan RA patients.

Visceral adiposity secondary to long term inflammation, usually seen in RA, has been implicated in the pathophysiology of Met-S and the associated insulin resistance (37). Other inflammatory conditions associated with increased risk of Met-S include osteoarthritis (38), systemic lupus erythromatosus (39) and HIV-AIDS (40). Increased visceral adiposity in RA has further been associated with sarcopenia and the attendant muscle loss has further been implicated in the pathogenesis of insulin resistance seen in Met-S (41,42). The association of Met-S with chronic inflammatory conditions has been attributed to the enhanced release of adipokines, including leptin, adiponectin and lipocalin-2, which drive the inflammatory process culminating in endothelial activation a precursor to atherosclerosis activation cascade (36,43). Inflammatory markers used in clinical evaluation of RA, and which have been associated with Met-S in RA (8,11), comprise C - reactive protein and erythrocyte sedimentation rate (34,36). How these parameters correlate with severity of the RA and the presence of Met-S for our local population, have however hardly been investigated. Similarly, the routine measurement of these parameters as markers of disease activity has locally not been established.

1.2.6 Hypertension in Rheumatoid Arthritis

Hypertension, a component of Met-S and a main modifiable risk for CVD, has been documented to occur quite frequently in RA patients relative to the general population (12,44). This observation has been attributed to the chronic inflammatory status with higher pressures being linked with a greater disease activity and elevated CRP (13,45). This prevalence of hypertension among RA patients has similarly also been shown to vary with the duration of the disease (8). The higher rates of hypertension in RA patients has been attributed to the multiple drugs taken to manage the disease. These drugs, including NSAIDs, have either been known to directly cause hypertension or negatively impact the effective control of hypertension (46). In one study, the prevalence of hypertension among RA patients was reported as 44%, twice the rate in matched controls (14). In the same study, target blood pressures for patients on treatment for hypertension were achieved in only 29% of patients.

Patients with RA have also been shown to have higher than normal ambulatory blood pressures and lower decline in the nocturnal blood pressure (14,45). Hypertension among RA patients, as with the general population and albeit at a greater rate, has also been positively been correlated with the increasing age and BMI of the patient (14,46). Other factors known to influence the prevalence of hypertension among RA is physical inactivity which is thought to be higher among these patients owing to the associated joint pain, stiffness and damage (46).

1.2.7 Dyslipidaemia and Hyperglycaemia in Rheumatoid Arthritis

Dyslipidaemia, that encompasses raised serum triglycerides (TG) and low high density lipoproteins, has been associated with higher rates of Met-S among RA patients (8,11,44). Similarly, various risk factors exist in RA patients that predispose them to T2DM. These consist of medications, including glucocorticoid use, and the chronic inflammatory state characteristic to RA (18,19). This is supported by observations that insulin resistance is observed in greater than 50% of patients with RA (47). Moreover, the presence of T2DM in females has been linked with an enhanced future risk of developing RA (48). However, use of methotrexate

and hydroxychloroquine in the treatment of RA has been linked with a reduction in the risk of getting type 2 diabetes (47,49). This occurrence has been attributed to the low grade inflammation associated with T2DM that predisposes genetically susceptible individuals to developing RA (50). Other studies have however reported that T2DM occurs more as a comorbid to RA and not as a risk factor (51). Despite all these observations, RA patients with T2DM have a double possibility of developing CVD relative to RA patients who do not have diabetes (47,52). Although dyslipidaemia has been recorded among patients with RA in our local populace (44), their association with disease severity has not been fully established.

1.2.8 Cardiovascular disease risk in rheumatoid arthritis

Patients with RA have been shown to have a higher CVD risk relative to unaffected patients. This risk is considerably higher in RA patients with concomitant Met-S and has been attributed to among other factors a greater degree of a sedentary lifestyle among RA patients with Met-S, severer disease among affected patients and a greater use of NSAID (53,54). Other factors that have been attributed to a greater CVD risk among RA patients are a delayed diagnosis and a longer duration of treatment (55).

Various scoring tools have been developed to estimate CVD burden. Among these is the ACC/AHA calculator that has been validated for use in patients above 40 years of age (56). Calculated scores are ranked as either low-risk, borderline, intermediate and high. Previous researchers have documented the CVD risk among RA patients with varying results attributed to among other factors the age of study participants, treatment duration and presence of comorbidities (57). However, hardly any estimates have been done for our local populace.

1.2.9 Rheumatoid Arthritis Disease Activity Scoring

Various scores, that combine single measures in to an overall one, have been developed for quantifying RA disease activity. These scoring systems include the Disease Activity Score-28 (DAS-28), Rheumatoid Arthritis Disease Activity Index (RADAI) and Rapid Assessment of Disease Activity in Rheumatology Index

(RADAR) (58,59). Of these scoring systems, the DAS-28 score has previously been used to document RA disease severity and is recommended for use by the American College of Rheumatology (60,61). DAS-28 score acts as a continuous estimate of RA disease activity incorporating measures that include acute phase response proteins (CRP/ESR), tender joints, swollen joints and the general health of the patient (62). Using this scoring system, RA disease activity is categorized in to either remission, minimal, moderate, and high activity (60). Higher RA disease activity scores have been linked with Met-S, an enhanced risk of CVD and a greater disability (63,64). Several freely accessible online calculators have been developed that can readily be used in a clinical setting to asses patients' disease activity (65).

1.3 Justification and Significance

The prevalence of RA in Africa and particularly in Kenya has been on an upward trend in the recent past (3,4). Relative to the greater population, persons living with RA have a greater mortality risk (23). Cardiovascular disease (CVD), of which RA patients have a two-fold greater risk relative to the greater population (24), has been identified as the commonest cause of mortality in these patients (1,25). Similarly, affected patients have higher 30-day mortality rates relative to non-RA patients following a newly diagnosed myocardial infarction or heart failure (26,27). Among the established causes of CVD in RA patients is metabolic syndrome (6). It was intended that the findings of this study would help in quantifying the burden of Met-S among RA patients attending rheumatology clinic in KNH.

1.4 Study question:

What is the burden and associated risk factors of metabolic syndrome among persons living with RA attending their clinic in a tertiary hospital in Kenya?

1.5 Broad objective:

To determine the prevalence, and associated risk factors, of metabolic syndrome among RA patients on followed up at the KNH Rheumatology Clinic.

1.6 Specific Objectives

1. To determine the prevalence of Met-S among patients living with RA
2. To determine the ASCVD score in patients with RA aged 40 years and above
3. To determine disease severity among RA patients using the DAS28-CRP scoring system

1.7 Secondary Objectives

1. To compare the prevalence of selected risk factors between RA patients with Met-S and those without Met-S

2. Materials and Methods

2.1 Study Design: A descriptive cross-sectional study

2.2 Study Site: This study was done on adult RA patients attending the Rheumatology Clinic at The Kenyatta National Hospital (KNH). KNH is a tertiary teaching hospital located in Nairobi. It runs weekly specialized clinics of which include the rheumatology clinic that runs every Tuesday and Thursday. The clinics are run by rheumatologists employed by both the KNH and the University of Nairobi and MMED in Internal Medicine registrars who are rotating in the Rheumatology Unit. The Principal Investigator (PI), who is an MMED in Internal Medicine Registrar, had already done his rotation in this clinic prior to commencing the data collection process.

2.3 Sample Size calculation

This being primarily a descriptive study, the sample size was determined using the following formula (66):

$n = Z^2P\ (1\text{-}P)/d^2$

Where

n = Sample size

Z = the statistic corresponding to 95% level of confidence

P = prevalence (prevalence of Met-S in RA from Bhattacharya's study was 36.5%) - (28)

d = precision

Prevalence of Met-S in RA patients for a study conducted in India was 36.5%. With a confidence level of 95% and an absolute precision of 10%, the sample size was thus calculated.

$n = 1.96^2 \text{ X } 0.365(1\text{- } 0.365)/0.1^2$

$n = 3.8416\ (0.365 \text{ X } 0.635)/0.01$

$n = (3.8416 \times 0.231775)/0.01$

$n = 0.89039/0.01$

$n = 89$

Thus, a minimum of 89 patients living with RA was required to conduct the study.

2.4 Selection and exclusion criteria

2.4.1 Patient Population

The study was done on patients with confirmed RA attending their clinics at the KNH. These patients were of diverse socioeconomic background and had been on follow-up at the clinic for different time durations. Most of the RA patients attending the adult rheumatology clinic are above 18 years of age and are drawn from various ethnic backgrounds.

2.4.2 Inclusion Criteria

All patients above 18 years of age on follow up for established RA, as defined by ACR/EULAR classification criteria for RA (67), were eligible for recruitment in to the study.

2.4.3 Exclusion Criteria

Patients with the following conditions were ineligible to participate in the study and were excluded:

1) Other autoimmune disorders
2) HIV-AIDS
3) Chronic liver & renal disease
4) Active malignancy
5) Patients with biochemistry laboratory results older than three months from the date of consenting to participate in the study

2.4.4 Recruitment of study participants

All suitable patients were then recruited in to the study until the minimum sample size was attained using the following criteria: the first registered RA patient was enrolled and thereafter, every third eligible patient.

The criterion was chosen to allow random selection of eligible patients into the study and thus minimise patient selection bias. They were informed of their eligibility to participate in the study after they had been attended to by their primary doctor. Individual interested patients (and their guardians when applicable) were then be taken to a separate consultation room for the consenting process. Patients who consented to participate in the study then had their relevant anthropometric and seating BP measurements taken. The BP measurement were taken twice with the patient seated and the left arm resting on the doctors' desk. The PI was then be left to extract the remaining laboratory data from the patient's file.

2.4.5 Data Collection Process

The following parameters were obtained, at the time of data collection and from the patients' files, for further use and analysis in the study:

1. Patient's sex, age, age at diagnosis, level of education (primary, secondary and tertiary) medications being used including dosages, height (m), weight (kg), waist circumference, CRP/ESR, blood pressure, fasting lipid profile and blood sugar and HbA1C levels. Blood pressure was taken using a digital BP machine by a trained research assistant twice (each reading five minutes apart) and the average taken. The weight of the patients was taken using a standard weighing scale accurate to 10g while a wall mounted height rod was used to take their heights. The laboratory values obtained for use in this study are routinely ordered as part of patient follow-up and thus no extra cost was incurred by the patient. For standardisation, only patients with lab results from the KNH laboratories were recruited.
2. Waist circumference was measured (in centimetres) at a point halfway between the inferior border of the ribcage and iliac crest (35).
3. Duration of disease was determined by subtracting patient's age at diagnosis from the current age of the patient.
4. Body mass index (BMI) was calculated as: mass (kg)/height^2 (meters).

5. Disease activity was assessed using the DAS28 (CRP/ESR) criteria (60) using the DAWN VISUAL DAS28 online calculator (65).
6. Ten-year atherosclerotic cardiovascular disease (ASCVD) risk for patients above 40 years of age was be estimated as per the 2013 ACC/AHA guidelines (56) utilizing the ASCVD Risk Estimator Plus calculator developed by ACC.

2.4.6. Case Definitions

1. Hypertension was defined as per the ESH/ESC hypertension guidelines and adopted by the Ministry of Health (MoH) (BP consistently ≥140/90 mm/Hg or patient already taking anti-hypertensive medications) (68).
2. Presence of diabetes was confirmed by the presence of either of: patient taking anti-diabetic drugs, HbA1C levels above 6.5%, a RBS of >11.1mmol/L or a FBS level >7.01mmol/L (69).
3. BMI was categorized as underweight (<18.5), healthy (>18.5 and <25), overweight (>25 and <30) or obese (>30) (70).
4. Ten-year risk for ASCVD was grouped as: low-risk (<5%), borderline (5% to 7.4%), intermediate (7.5% to 19.9%) and high (≥20%).
5. RA disease activity level was graded into four categories: remission (DAS28 ≤2.6), low/minimal (2.6 <DAS28≤ 3.2), moderate (3.2 < DAS28 ≤ 5.1) and high disease activity (5.1> DAS28) (60).
6. Presence of Met-S was ascertained by the presence of any three of these five features (71):
    a. Increased waist circumference (≥ 102 cm for men and ≥ 88 cm for women)
    b. Elevated BP (≥140/≥90 mmHg)
    c. High triglyceride levels (≥1.7 mmol/L) or medical therapy for elevated TG
    d. Low HDL-C (< 1.03 mmol/L for male patients and < 1.3 mmol/L for female patients)
    e. Elevated FBS (>7.01mmol/L), RBS (>11.1mmol/L) and/or HbA1C level (>6.5%), or medical therapy for raised glucose

Only laboratory test results (for HbA1C, FLP, RBS) all reported on the same day for a particular patient were used in this study to determine presence/absence of Met-S. Standardization of the methods used to measure the various analytes of the results used in this study was guaranteed by the fact that only results obtained from the KNH laboratory were used in this study. The laboratory uses the same machines to run the respective analytes and has an up to date quality control protocol whose adherence is regularly monitored. Similarly, reagents used for all analysis are sourced from reputable institutions that are vetted prior to supply of the reagents.

Patients were then grouped to those with Met-S and those without Met-S (control).

2.4.7 Study Tools

a. Patient's weights were taken using the electronic Von VSWE18MCX weighing scale manufactured by HotPoint Appliances Limited. It can measure up to 180kg and has a sensitivity of 10g.
b. Waist circumference was taken using a standard 2M-long tape measure with a sensitivity of 1cm.
c. Patients' heights were measured using wall mounted height rod manufactured by SOEHNLE. This can measure up to 3 meters and has a sensitivity of 1cm.

2.4.8 Quality Assurance Protocol

Two Research Assistants recruited to help in the data collection process were trained on the procedures stated above. All anthropometric measurements were taken twice by each research assistant and the average of their readings taken as the final score. The PI ensured adherence to the study protocol at every stage. Only laboratory results from KNH were used in the scoring of the Met-S. The assistants were required to do the free online ICH Good Clinical Practice E6 by the Global Health Training Centre before they participated in the data collection process. They were also be trained by the PI on how to take the patients' heights, weights and abdominal circumference as per the protocol guidelines.

2.5 Ethical Considerations

The proposal for the study was presented to the Department of Clinical Medicine and Therapeutics and approved. Ethical approval to conduct the study was then sought from and granted by the KNH-UON Ethics and Research Committee. Subsequently, we sought and got institutional approval to conduct the study from the office of the Director of Clinical Services, KNH. Informed consent was then obtained from all study participants by the PI before they were recruited to partake in the study. Participation of subjects in this study was entirely voluntary. For anonymity of study participants, no actual names were captured anywhere along the data collection and handling process. Study participants were however assigned numerical numbers which have been used as their identifiers. All laboratory tests used in this study are part of what is routinely done as follow up for RA disease management, and thus no additional costs were levied to the patients.

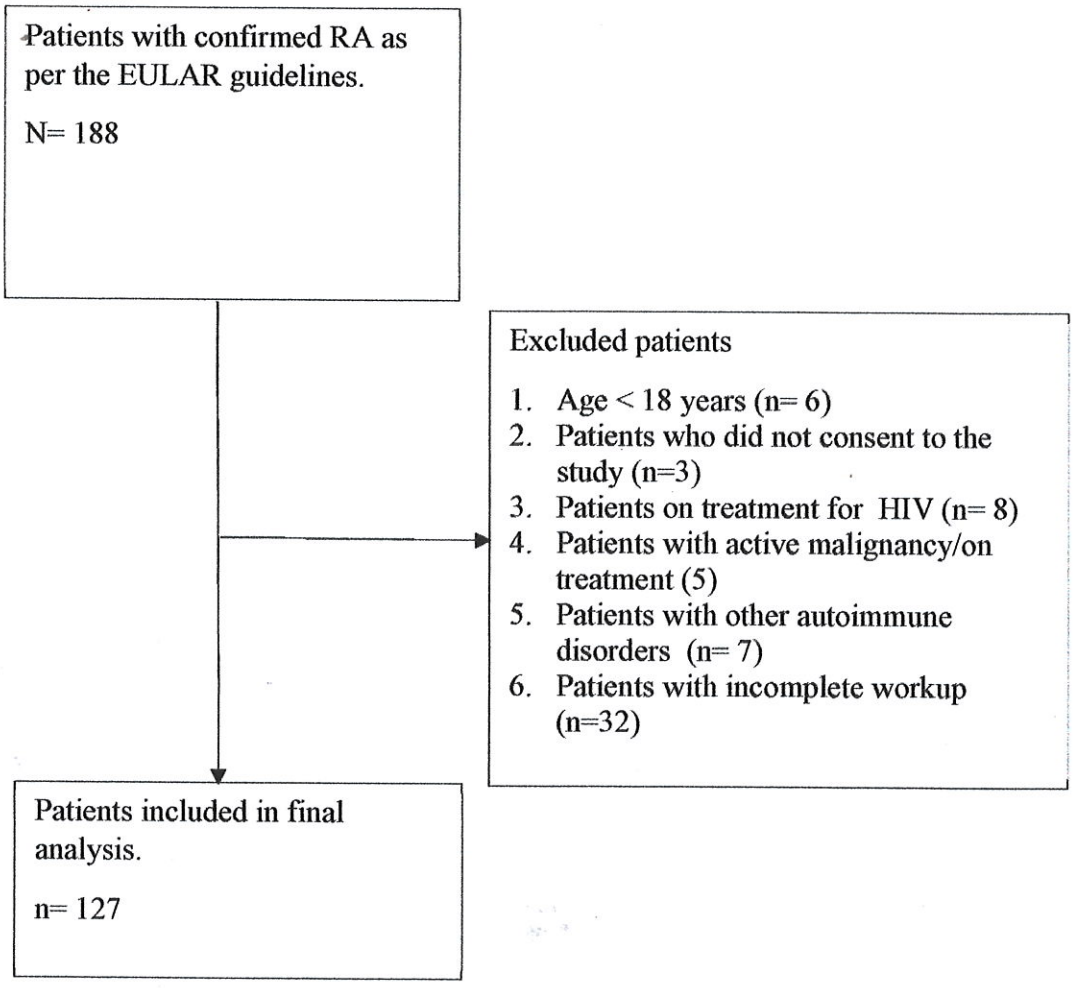
2.6 Data analysis and Management

Analysis of the data was carried out using SPSS (Version 25, New York, USA). Categorical data was reported as frequencies (%), whereas continuous data was subjected to normality tests and appropriate statistical techniques applied. Graphs and tables were used to summarise data with continuous data expressed in means and standard deviation. Independent Student's-t test was used for comparison of quantitative/numerical patient and disease characteristics (age, age at diagnosis, BMI, waist circumference, duration of disease, CRP/ESR, fasting lipid profile, blood sugar/HbA1c levels) between patients with Met-S and those without Met-S (control group). Comparison of categorical data (disease activity, sex, medication use e.g., corticosteroids, methotrexate) was carried out using Chi-square test. Logistic regression was performed to estimate the impact of moderator variables (disease duration, disease activity, CRP levels, methotrexate use, steroid use and NSAID use), adjusting for age, sex and baseline characteristics. Further variable selection and model improvement was performed using the stepwise algorithm. Final logistic models were used to calculate adjusted odds ratios (ORs) with the corresponding 95% Wald confidence interval (CI). Throughout the analysis, a $p<0.05$ was considered statistically significant at a 95% CI.

3. Results

The present study was carried out between June and November 2022. A total of 188 patients met the inclusion criteria while 61 were excluded (Flow Chart 1). Of the excluded patients 6 were below 18 years of age, 3 did not consent, 6 had HIV while 5 were on treatment for a malignancy (currently or in the past one year) - three were on treatment for breast cancer while one was on treatment for thyroid cancer and another for gastrointestinal-related malignancy. Three patients had coexisting SLE and were thus excluded as were 4 who were on follow up for suspected small vessel vasculitis. Of the patients with incomplete workup, 4 were newly diagnosed patients, 15 had misplaced files while 13 had not been worked up for more than 1 year.

Flow Chart 1: Chart showing patient recruitment in to the study



3.1 Patient Demographics and Clinical Characteristics

Of the 127 patients who participated in the study, 115 were female (90.6%) while 12 were male. The mean age was 51.48±15.7 years (range 18 to 83 years) while the average age at diagnosis was 43.29±13.81 years (range 15 to 74 years). Of the enrolled patients, 97 (76.38%) were above 40 years of age (83.3% of men and 75.65% women). The recruited patients had been on treatment for RA for a median of 6.65 years with a majority of the patients (74%) having been on follow up for 10 years or less (Table 1). Fifty-five patients (43.3%), including 53 female patients, only had primary level of education with 32 patients (25%) and 40 patients (31.5%) having attained secondary and tertiary level of education respectively. A greater proportion of male participants (83.33%) however, had tertiary level of education compared to only 26.09% of female patients. None of the patients had a previous history of smoking or cerebrovascular (CVA) accident. Forty-four patients (34.6%) were on various NSAIDS, 73 (57.5%) were on steroids while 89 patients (70.1%) were on methotrexate. It was however, not possible to determine how long these patients had been on these drugs.

Table 1: Table showing summaries of various study parameters

Parameter	Mean
Age (Years)	51.48±15.71
Age at Diagnosis (Years)	43.29±13.81
Waist Circumference (cm)	91.89±7.91
SBP (mmHg)	131.11±18.78
DBP (mmHg)	79.21±11.2
CRP*	7.1
ESR (mm/Hr)*	30.8
RBS (mmol/dL)	5.66±1.52
HbA1C	5.99±2.22
DAS28	3.483±1.17
BMI (Kg/M^2)	26.21±3.68
Total Cholesterol (mg/dL)	166.33±34.96
HDL (mg/dL)	48.59±12.29
TG (mg/dL)	112.29±46.06

* Median

3.2 Metabolic Syndrome RA Patients

A total of 27 patients (21.26%) met the criteria for METS (25 female and 2 male patients). A majority of the patients with METS only had primary level of education (77.8%) compared to the almost uniform distribution across all levels of education for RA patients without METS (Table 2). A bigger proportion of patients with METS had greater WC, SBP, and TG levels and were more likely to be hypertensive and diabetic. These patients were likely to be overweight or obese (78% vs. 53% for patients without METS).

Table 2: Table showing summaries of the various components of METS

Parameter	N (out of 127)	%
Patients with WC above cut-off	83	65.35
BMI (overweight & Obese patients)	74	58.27
Patients with HTN	68	53.54
Patients with DM	18	14.17
Patients with Dyslipidaemia	38	29.92
Patients with METS	27	21.26

3.3 Adiposity in Rheumatoid Arthritis

Eighty-three patients (65.4%) had a waist circumference above the set cut off while 58 (45.7%) and 16 (12.6%) were overweight and obese respectively. Additionally, 80% of patients with primary level of education had an increased WC compared to 59.4% of patients with secondary education and 50% of patients with tertiary education. Forty-nine (59.04%) of the 83 patients on steroids had increased WC while 54.54% of patients not on steroids had a WC above the set cut-off.

3.4 Hypertension in Rheumatoid Arthritis

Sixty-eight patients (53.5%) were hypertensive (59 female and 9 male). A majority of these patients (76.47%) had uncontrolled BP. Patients with hypertension were much older, had a later age at diagnosis and had longer disease duration. A third of these patients with HTN (33.8%) were not on any anti-hypertensive medication while those on treatment were on either one or two anti-hypertensive drugs (34.78% and 52.17% respectively). Only one third of these patients with HTN were on NSAIDs and only 25% of them had DM as a comorbidity. Moreover, more patients with primary level of education were hypertensive compared to those with secondary and tertiary level of education.

3.5 Diabetes in Rheumatoid Arthritis

Eighteen (14.17%) patients (16 female and 2 male) were diabetic and all were on treatment. DM patients were considerably older, were older at diagnosis and had had a longer duration of RA treatment. Of these DM patients, 16 were female while 2 were male and all had type 2 DM. Only five of the diabetic patients (27.8%) had not achieved glycaemic control. Nine (50%) of the diabetic patients were on steroids compared to 64 (58.72%) non-diabetic patients.

3.6 Dyslipidaemia in Rheumatoid Arthritis

Dyslipidaemia was found in 38 (29.9%) patients (34 female and 4 male) with 23 (18.1%) patients having elevated TG levels while 15 (11.8%) participants had low HDL levels. Only 10 patients were on anti-lipidemic medicines while 5 patients were on lipid-lowering drugs despite recording a normal lipid profile. Compared to female patients, male patients had on average lower HDL levels but higher TG and TC levels.

3.7 Cardiovascular Disease Risk in Rheumatoid Arthritis

Of the 97 patients aged above 40 years, only 33 (34.02%) had a low 10-year CVD risk score while a considerable number had either intermediate or high-risk scores (52.58%) - Figure 1. None of the participants had a positive history of cigarette smoking nor previous stroke.

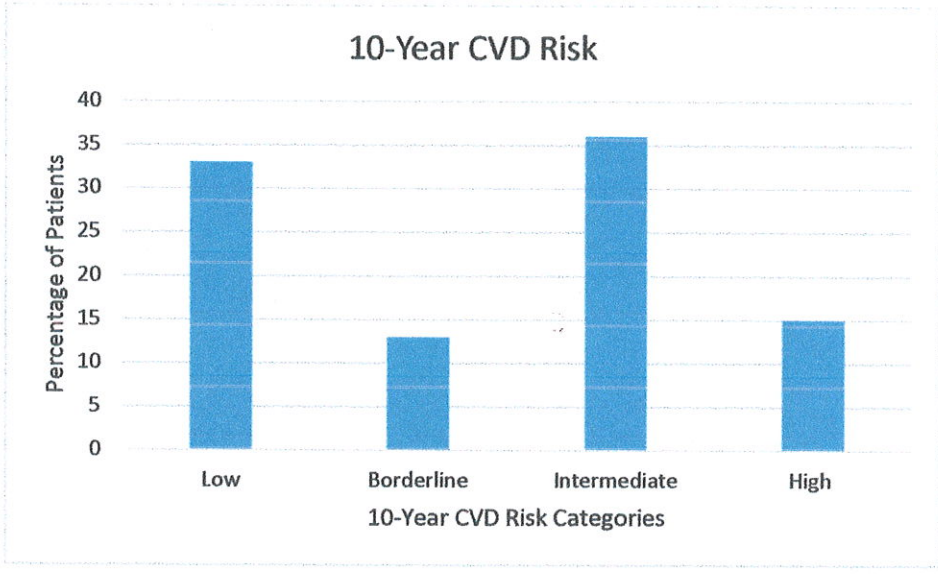


Figure 1: Graph showing the 10-year CVD risk categories

3.8 Rheumatoid Arthritis Disease Severity

The median CRP level was 7.1 µ/mL while that of the ESR (for 59 patients) was 30 mm/Hr. Similarly, and as marked by the DAS28 scores, a majority (55.12%) of the patients had either moderate or high disease activity compared to the 44.88% of the participants who had either a low or remission category of disease severity (Figure 2). A majority of the patients under study were either on 1 or 2 DMARDS (39.4% and 51.2% respectively). On the other hand, two patients were not any DMARDS while 1 patient was on 4 DMARDS. The most commonly prescribed DMARDS were methotrexate (prescribed in 89 patients - 70.1%) and various steroid formulations (used by 73 patients - 57.5%). NSAID prescriptions were encountered in only 44 (34.6%) patients. Likewise, a greater proportion of patients with primary level of education had either intermediate or high level of RA disease activity.

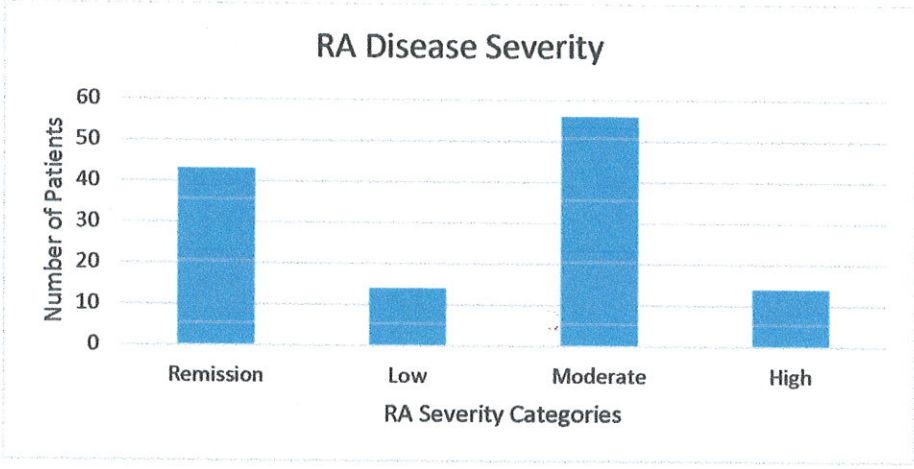


Figure 2: Graph showing number of patients per RA disease category

3.9 Comparison of Selected Parameters for RA Patients with and without METS

Explorative inferential analysis was done to elucidate the differences between patients with and without METS and whether these differences would predict the risk to METS. Patients with METS were found to be significantly older, had had a later age of diagnosis and a longer duration of treatment ($p<0.001$). All the patients with METS were above 40 years of age and had significantly greater SBP, WC, RBS, TC (all $p<0.001$), HbA1C ($p=0.012$), BMI ($p=0.002$), and TG ($p=0.003$) - Table 3. Similarly, RA patients with METS had a higher RA disease activity (70.4% vs. 51%) - (figure 3) and a bigger percentage of these patients had a greater 10-year CVD risk (intermediate and high risk) compared to RA patients with no METS (77.8% vs. 42.85%) - Figure 4. Furthermore, more patients with Met-S were likely to be on NSAIDs and steroids.

Table 3: Table showing differences in continuous variables between patients with METS and those without METS

Parameter	METS (n=27)	No METS (n=100)	p-value
Age	65.56±11.33	48.22±15.16	**<0.001**
Age at Diagnosis	51.78±9.49	41.00±13.94	**<0.001**
Duration of Disease	15.3	5.9	**<0.001**
Waist Circumference	98.89±9.61	90±6.18	**<0.001**
CRP*	15.06	8.9	0.369
ESR*	45.3	30.8	**0.039**
SBP	146.33±17	129.55±17.67	**<0.001**
DBP	77.78±11.06	79.6±11.26	0.454
RBS	7.38±2.38	5.2±0.66	**<0.001**
HbA1C			
BMI	28.56±4.19	25.58±3.28	**0.002**
Total Cholesterol	197.17±49.64	158.01±24.07	**<0.001**
HDL	47.05±12.05	49.01±12.39	0.461
TG	141.58±57.07	104.39±39.34	**0.003**

*median. Bold is statistically significant

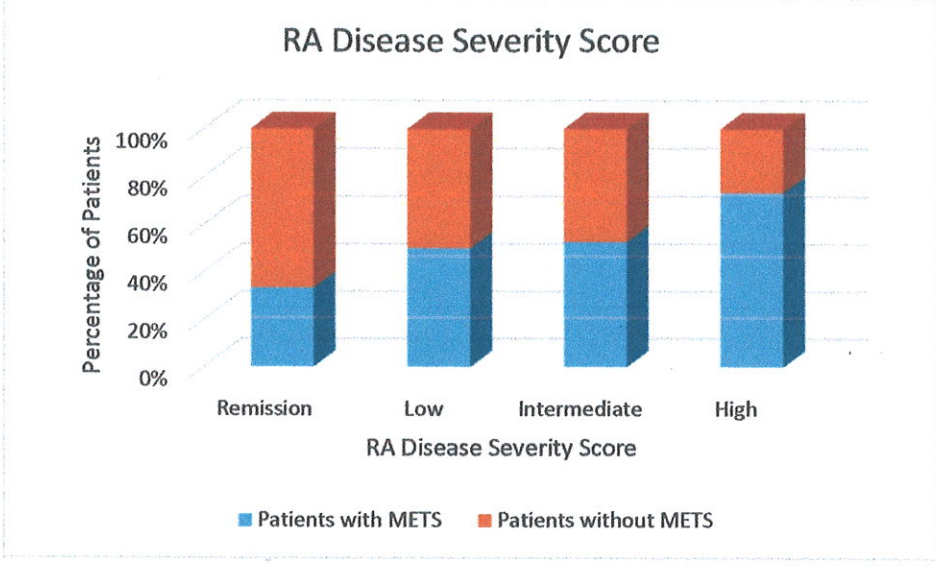


Figure 3: Graph showing differences in RA disease severity between patients with METS and those without METS

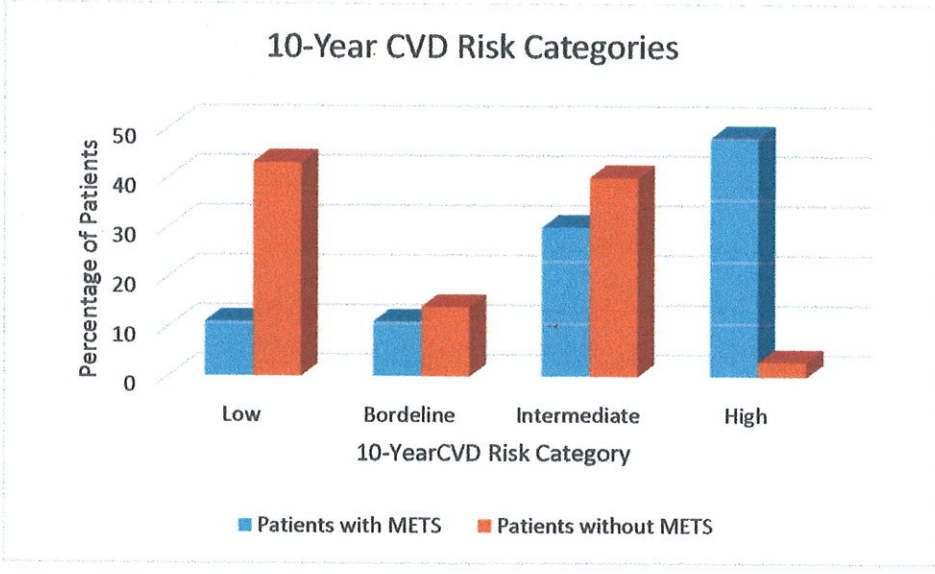


Figure 4: Graph showing differences in 10-year CVD risk between patients with METS and those without METS

3.10 Results for Logistic Regression Analysis

Univariate (unadjusted analysis), age at diagnosis (OR= 1.07, p<0.001), disease duration (OR= 1.08, p=0.004), disease activity (OR= 1.76, p=0.004), elevated CRP (OR= 1.01, p=0.021) and steroid use (OR= 2.90, p=0.018) were associated with metabolic syndrome (Met-S). After adjusting for potential confounders, age at diagnosis (OR= 1.08, p= 0.007), disease duration (OR= 1.08, p=0.030), elevated CRP (OR= 1.02, p=0.040) and steroid use (OR= 3.75, p=0.035) remained as significant predictors of development of Met-S (Table 4).

Table 4: Table showing results for logistic regression analysis for the various parameters under consideration

Variable	Crude OR (95% CI)	Adjusted OR (95% CI)
Age at diagnosis	1.07 (1.03-1.12), ***p<0.001***	1.08 (1.02-1.14), ***p=0.007***
Sex (male)	1.39 (0.029-6.75), *p=0.684*	3.42 (0.55-21.28), *p=0.188*
Disease duration	1.08 (1.02-1.14), ***p=0.006***	1.08 (1.01-1.16), ***p=0.030***
DAS28	1.76 (1.19-2.60), ***p=0.004***	1.75 (1.00-3.06), *p=0.051*
CRP	1.01 (1.00-1.08), ***p=0.021***	1.02 (1.00-1.04), ***p=0.040***
Methotrexate use	1.28 (0.49-3.35), *p=0.610*	1.09 (0.34-3.52), *p=0.891*
Steroid use	2.90 (1.20-6.98), ***p=0.012***	3.95 (1.10-12.82), *p=**0.035***
NSAID use	2.81 (0.98-8.05), *p=0.054*	1.78 (0.52-6.09), *p=0.357*

Bold: statistically significant

4. Discussion

The prevalence of RA in Africa and particularly in Kenya has been on an upward trend in the recent past (3,4). Affected patients have a lower quality of life and are at an increased risk of cardiovascular disease and mortality emanating from enhanced CVD, of which RA patients have a two-fold greater risk relative to the greater population (1,25). Among the established causes of CVD in RA patients is METS (6). However, the prevalence of METS varies from one study cohort to another and had hitherto not been established for our local population. We further endeavoured to elucidate the predictors of METS among RA patients.

4.1 Patient Characteristics

The current study reported a disproportionately higher number of female patients (F:M=9:1) compared to the 6:1 ratio reported in an earlier meta-analysis of studies done from Africa (15). Nonetheless, our findings are similar to results from Asian studies (72,73) and the findings might be attributed to a poorer health-seeking behaviour among male patients and misdiagnosis of RA as other arthropathies, especially osteoarthritis, among these patients (74,75). Furthermore, RA is an autoimmune inflammatory disease that mainly affects women with variably reported prevalence rates ranging from a low of 52% to a high of 100% (46,76). This female preponderance of RA is however age dependent with past studies documenting that RA occurs up to 4-5 times higher in women for cohorts below 50 years of age with this ratio reducing to 2:1 in patients above 60-70 years (77).

Majority of the participants in the current study had an advanced age at diagnosis, a longer duration of treatment and primary level of education. A dearth of awareness of connective tissue diseases coupled with a lower number of trained rheumatologists in Africa has in the past been attributed not only with the low prevalence of rheumatic diseases in the continent but also a later age of diagnosis (15). Similarly, delays in specialist referrals for RA patients of up to 12.9 years have been reported in previous African studies contrasting starkly with the delay of between 1 and 3 months reported in studies from western Europe (15,78). This might further explain the higher average age at diagnosis seen in our patients compared to studies done

among European and affluent Asian countries (3). This late diagnosis of RA has been associated with greater disease activity and delayed initiation of DMARDS, and as likewise seen in our analysis, the predisposition to the various components of METS (79). However, recent improvement in patient care has resulted, as reflected in our findings, in patients living with RA for long with a considerable number of patients being treated for the disease for more than 20 years.

A great proportion of our participants, especially women, had only primary level of education. A low level of education, a marker of low socioeconomic status, has in the past been associated with severer RA disease activity and limited access to DMARD therapy (73,80,81). This has been attributed to the positive influence that advanced formal education has on patient attitudes towards health seeking behaviour, adherence to prescribed medications and access to medical care (80,82). Similarly, a greater percentage of patients in our study who only had primary level of education tended to have either moderate or high RA disease activity. These patients were also older and had a propensity to METS, including being overweight and obese, compared to patients with higher academic qualifications.

4.2 Metabolic Syndrome among Patients with Rheumatoid Arthritis

Even though the prevalence of METS in RA occurred in about 21% of the participants, some of the individual components were more prevalent including measures of adiposity (WC above set cut-off 65% and unhealthy BMI 58%) and HTN (54%). The global prevalence of METS in RA has been estimated at 32% (range 8.2% to 44%) but shows significant regional differences with the highest rates reported in Asia and Europe while studies from Africa report lower rates with an average prevalence of 28% (range 14% to 33.2%) (10,83). The reported prevalence in the current study (21.26%), though lower than the African average, is higher than the 18% reported in a Moroccan study (34). Past research on METS in RA has attributed this discrepancy in the prevalence rates to the selection of the cut-offs for the various components of METS, the exact definition of METS used and age heterogeneity of study participants in the various published works (34,83). The burden

of METS in RA can, however, not be ignored since it increases adverse cardiovascular outcomes by 2 times and enhances mortality risk by 1.5 times (83).

The observation in the current study that patients with METS were likely to have greater disease activity, an advanced age at diagnosis, and have had a longer duration of RA treatment has been variably reproduced in the past (10,84,85). Similarly, and as previously reported, male sex and the use of methotrexate and NSAID did not seem to predispose patients to METS (32,34). Nonetheless, a high inflammatory habitus as reflected by high DAS-28 scores and raised CRP values, was strongly correlated with predisposition to METS. This observation has been seen with other joint diseases including osteoarthritis and has been shown to precipitate insulin resistance and reduced vascular compliance exposing RA patients to components of METS (86). Furthermore, affected patients tend to have a high disease activity resulting in chronic pain, reduced physical activity and eventually a sedentary lifestyle (9).

We further showed, as reported in past publications, that various components of METS occur at varied frequencies independent of each other and whether or not the patient has METS (10). This observation is further compounded by the realization that a majority of METS components in the current study, including HTN and markers of visceral adiposity, were poorly controlled. The need to modify for the risk factors for METS in RA can therefore not be overemphasized.

4.3 Adiposity in Rheumatoid Arthritis

A majority of the participants in the current study had a WC above the set cut-off (65%) or were either overweight or obese (58%). Furthermore, affected patients were found to have a higher RA disease activity, as reflected by high DAS-28 scores and higher CRP levels, and on steroid prescription. A sedentary lifestyle necessitated by immobility from poorly controlled RA coupled with steroid use among these patients has been blamed for the high prevalence of adiposity (18). Male participants in the current study were nonetheless found to have healthier BMI and less were above the WC cut-off compared to female participants. This is in

contrast to previous findings that report male RA patients having greater BMI compared to female patients (87,88). However, the findings of the current could possibly be a case of RA-associated cachexia seen in severe RA disease since the male patients were also found to have greater DAS28 scores and CRP values (89).

4.4 Hypertension in Rheumatoid Arthritis

Over half of our patients (53.5%), were hypertensive which was similar to findings of an American study (53.3%, n=169) (90) but higher than the 32.5% (n=1490) reported in an Asian study (91). A past systematic review has placed the prevalence of HTN in RA to range between 3.8% and 77.5% (46) with increased mean arterial BP among RA patients being independently associated with arterial stiffening and thus placing these patients at an enhanced risk for CVD (92). The high rates of HTN among RA patients has in the past been positively associated with increasing age and longer duration of disease but not with DM, NSAID use and markers of systemic inflammation (90). Similar observations have been reported not only in RA but also other inflammatory conditions including SLE (93). Our findings support this observation since our hypertensive patients were significantly older, had a late RA diagnosis and had been on treatment for longer. Furthermore, only 25% of the HTN patients were diabetic and there was no difference between hypertensive and non-hypertensive patients in terms of the inflammatory markers and NSAID use. Other factors that have been known to modulate the development of HTN among RA patients and that were not found to have association in the current study include use of methotrexate and steroids (94). The development of HTN among RA patients thus seems to be independent of the disease and more about advancing age. Further research on the risk factors is thus, warranted. Moreover, suboptimal BP control was found in more than three quarters of the hypertensive patients included in this study, a figure that is similar to the 71% reported in a previous study (14). Maximization of BP control would however diminish this risk easily modifiable CVD risk factor.

4.5 Diabetes and Rheumatoid Arthritis

At 14%, diabetes was the least prevalent of the METS components. A previous study (N=100) similarly documented the prevalence of undiagnosed DM in RA at 10% with the risk being positively associated with being older and having a longer disease duration (95). This in keeping with findings of the current study where affected patients were older and had been on treatment for longer. We further found that patients with DM were likely to have had a later age of RA diagnosis relative to non-diabetic patients. A larger international study (N=10543) recorded a prevalence of 13% and further reported that RA patients with DM were also likely to have HTN and dyslipidaemia (96).

The role of DMARDS like HCQ and MTX in reducing the risk of DM in RA has been suggested before but the evidence is not entirely conclusive (49,97). Similarly, there was no proportional difference in steroid and MTX use between patients with and those without DM. Nevertheless, the increased risk of developing DM among RA patients is partly mediated by the inflammatory milieu and insulin resistance found in over 50% of affected patients (47,98). This was similarly reflected in our findings where high CRP and DAS-28 scores among RA patients predisposed them to METS in general and DM in particular.

4.6 Dyslipidaemia and Rheumatoid Arthritis

Dyslipidaemia was found in about 28% of the study participants which is much lower than reported in studies from Asia. For instance, a Japanese study (n=488) reported the prevalence of dyslipidaemia was 56.5% which was associated with high DAS28 scores and treatment with glucocorticoids (99). A study from Pakistan (n=200) reported a similar prevalence of 53.5% with the commonest lipid profile abnormality being low HDL-C (72). Our findings however closely mirror those of an earlier Dutch study (100) and are in keeping with a more recent South African study that reported that reduced dyslipidaemia in RA patients was associated with a reduced BMI (89). Other investigators have placed the prevalence of dyslipidaemia to be between 30% and 40% with all studies done in different settings and countries and with varied number of

participants (101,102). In a different study, post prandial hyperlipidaemia was more prevalent among RA patients (38.7% vs. 22.4%) compared to age- and sex-matched controls (103).

Dyslipidaemia in RA has been thought to occur in early RA or even precede its diagnosis (104). Its aetiology is partly linked to the increased visceral adiposity preferentially found in majority of RA patients compared to matched controls. The inflammatory environment in RA further causes lower HDL-C and impairs with its athero-protective function as evidenced by the dyslipidaemia found in patients with RA cachexia (87). Moreover, dyslipidaemia related to glucocorticoid use has been shown to be dose-dependent and is initially attributed to elevated HDL-C without an attendant increase in the atherogenic cholesterols (105). The current study did not however investigate the effect of glucocorticoid therapy in RA since the patients were on different molecules and dosages. Furthermore, it was difficult to establish how long the patients had been on the prescribed steroids. Nevertheless, patients on steroids had lower TC and TG levels compared to those who were not on any steroids. Other factors that have been known to variably influence the lipid profile in RA patients include duration of disease, the patients' age, a sedentary lifestyle and use of biologic DMARDS and ACE-inhibitors (99,100,102).

4.7 Atherosclerotic Cardiovascular Disease Risk among Patients with Rheumatoid Arthritis

Patients with RA have been known to have an enhanced risk of CVD relative to the general population. The up to 2-fold risk emanates from the additive effects of the chronic inflammation and the numerous CVD risk factors that are preferentially found in these patients (53). The overall ASCVD score for the current study was slightly lower than a scores reported in other studies done mainly among a Caucasian population (54,57). Similarly, another study (N=84) found that 39.3% of RA patients had high CVD risk scores compared to the 15% reported in the current study (106). The higher risk scores in the past studies might be explained by the observation that most of the studies had some of their participants being active smokers unlike the present study where none of the patients had a positive history of smoking nor a past CVA.

High CVD risk scores in RA patients reflect subclinical atherosclerosis and have been correlated with other markers of atherosclerosis including carotid intima-medial thickening and calcification of coronary arteries (107,108). These findings further put affected patients at the risk of CVA and myocardial infarctions, conditions known to be more prevalent among RA patients relative to the general public. The risk of CVD is higher among male patients and those with a severer inflammatory status as reflected by high DAS-28 scores and greater CRP and ESR readings (55). This observation is reflected in the current study where men had higher DAS-28 scores and CRP levels. As such, additional screening for subclinical atherosclerosis, including use of carotid Doppler ultrasound, have been routinely recommended since there is an apparent fear that most of the ASCVD screening scores might actually underestimate the burden on CVD risk in RA as most were developed for use in non-rheumatologic patients (109).

4.8 Rheumatoid Arthritis Disease Activity

Rheumatoid arthritis disease activity has traditionally been reported to be worse among female patients compared to male patients (110,111). On the contrary, male patients in the current study had greater DAS28 scores and were characterised with more joint deformities and tenderness besides having higher CRP and ESR readings. The higher inflammatory marker values recorded in the male compared to female patients further points to a more inflammatory milieu that explains the higher disease activity recorded among male patients in the current study. Consequently, male patients had higher CVD risk scores. This was in spite of the fact that none of the male patients in the current study had a positive history of smoking, a known determinant of adverse disease activity and CVD among RA patients (112,113). The current study was nevertheless done in an apex referral hospital that treats patients with likely advanced disease, which, coupled with the smaller number of recruited male patients who might have had severer disease, would explain this deviation from the norm. Nonetheless, our study findings are concordant with findings of a larger, more recent Chinese study that found that male patients had a more active disease with higher DAS28 scores, inflammatory markers and a propensity to adverse outcomes including strokes and CAD (114). Furthermore,

female patients with greater CRP and DAS28 scores were likely to have METS, a finding that has prior been reported by various authors.

5. Conclusion

Despite prevalence of METS being lower than the global average, a majority of the components of METS were highly prevalent and many patients had advanced RA disease activity. There was also sub-optimisation of many of the easily modifiable risk factors including obesity and hypertension. This placed affected patients at higher risk for CVD. Greater emphasis during follow up should therefore be accorded to RA patients in order to identify and manage easily modifiable risk factors including obesity, HTN and dyslipidaemia.

5.1 Study Limitations and Delimitations

1. Selection bias since the study was done in a tertiary hospital with participating patients probably having severe disease since KNH is a referral hospital. The participants however represent the patients mostly encountered in our country.
2. Missing study variables made us exclude 32 (17%) potential study participants. This did not however affect our sample size that had been estimated initially at 89.

6. References

1. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. Nat Rev Dis Primer. 2018 Feb 8;4(1):1–23.

2. Peschken CA, Hitchon CA, Robinson DB, Smolik I, Barnabe CR, Prematilake S, et al. Rheumatoid Arthritis in a North American Native Population: Longitudinal Followup and Comparison with a White Population. J Rheumatol. 2010 Aug 1;37(8):1589–95.

3. Almoallim H, Al Saleh J, Badsha H, Ahmed HM, Habjoka S, Menassa JA, et al. A Review of the Prevalence and Unmet Needs in the Management of Rheumatoid Arthritis in Africa and the Middle East. Rheumatol Ther. 2021 Mar 1;8(1):1–16.

4. Safiri S, Kolahi AA, Hoy D, Smith E, Bettampadi D, Mansournia MA, et al. Global, regional and national burden of rheumatoid arthritis 1990-2017: a systematic analysis of the Global Burden of Disease study 2017. Ann Rheum Dis. 2019 Nov;78(11):1463–71.

5. Alberti K g. m. m., Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the Metabolic Syndrome. Circulation. 2009 Oct 20;120(16):1640–5.

6. Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Med. 2011 May 5;9(1):48.

7. Omuse G, Maina D, Hoffman M, Mwangi J, Wambua C, Kagotho E, et al. Metabolic syndrome and its predictors in an urban population in Kenya: A cross sectional study. BMC Endocr Disord. 2017 Jul 4;17(1):37.

8. Chung CP, Oeser A, Solus JF, Avalos I, Gebretsadik T, Shintani A, et al. Prevalence of the metabolic syndrome is increased in rheumatoid arthritis and is associated with coronary atherosclerosis. Atherosclerosis. 2008 Feb;196(2):756–63.

9. da Cunha VR, Brenol CV, Brenol JCT, Fuchs SC, Arlindo EM, Melo IMF, et al. Metabolic syndrome prevalence is increased in rheumatoid arthritis patients and is associated with disease activity. Scand J Rheumatol. 2012 May;41(3):186–91.

10. Hallajzadeh J, Safiri S, Mansournia MA, Khoramdad M, Izadi N, Almasi-Hashiani A, et al. Metabolic syndrome and its components among rheumatoid arthritis patients: A comprehensive updated systematic review and meta-analysis. PLOS ONE. 2017 Mar 23;12(3):e0170361.

11. Pandey PK, Swami A, Biswas TK, Thakuria R. Prevalence of Metabolic Syndrome in Treatment Naïve Rheumatoid Arthritis and Correlation With Disease Parameters. Arch Rheumatol. 2017;32(1):046–52.

12. Karimi M, Mazloomzadeh S, Kafan S, Amirmoghadami H. The frequency of metabolic syndrome in women with rheumatoid arthritis and in controls. Int J Rheum Dis. 2011;14(3):248–54.

13. Pope JE, Choy EH. C-reactive protein and implications in rheumatoid arthritis and associated comorbidities. Semin Arthritis Rheum. 2021 Feb;51(1):219–29.

14. Protogerou A, Zampeli E, Konstantonis GD, Arida K, Panagiotakos DB, Argyris AA, et al. SAT0073 Arterial Hypertension In Rheumatoid Arthritis Without Cardiovascular Disease: High Prevalence, Low Awareness, Poor Control And Increased Vascular Damage-Associated "White Coat" Phenomenon. Ann Rheum Dis. 2013 Jun 1;72(Suppl 3):A604–A604.

15. Adelowo O, Mody GM, Tikly M, Oyoo O, Slimani S. Rheumatic diseases in Africa. Nat Rev Rheumatol. 2021 Jun;17(6):363–74.

16. Jiang X, Alfredsson L. Modifiable environmental exposure and risk of rheumatoid arthritis-current evidence from genetic studies. Arthritis Res Ther. 2020 Jun 22;22(1):154.

17. Silva-Fernández L, Macía-Villa C, Seoane-Mato D, Cortés-Verdú R, Romero-Pérez A, Quevedo-Vila V, et al. The prevalence of rheumatoid arthritis in Spain. Sci Rep. 2020 Dec 9;10(1):21551.

18. Ohno T, Aune D, Heath AK. Adiposity and the risk of rheumatoid arthritis: a systematic review and meta-analysis of cohort studies. Sci Rep. 2020 Sep 29;10(1):16006.

19. Tang B, Shi H, Alfredsson L, Klareskog L, Padyukov L, Jiang X. Obesity-Related Traits and the Development of Rheumatoid Arthritis: Evidence From Genetic Data. Arthritis Rheumatol Hoboken NJ. 2021 Feb;73(2):203–11.

20. Usenbo A, Kramer V, Young T, Musekiwa A. Prevalence of Arthritis in Africa: A Systematic Review and Meta-Analysis. PLoS ONE. 2015 Aug 4;10(8):e0133858.

21. Hunter TM, Boytsov NN, Zhang X, Schroeder K, Michaud K, Araujo AB. Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004-2014. Rheumatol Int. 2017 Sep;37(9):1551–7.

22. Elshafie AI, Elkhalifa AD, Elbagir S, Aledrissy MIE, Elagib EM, Nur MAM, et al. Active Rheumatoid Arthritis in Central Africa: A Comparative Study Between Sudan and Sweden. J Rheumatol. 2016 Oct 1;43(10):1777–86.

23. Otón T, Carmona L. The epidemiology of established rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2019 Oct;33(5):101477.

24. Liao KP. Cardiovascular disease in patients with rheumatoid arthritis. Trends Cardiovasc Med. 2017 Feb;27(2):136–40.

25. Faden G, Viapiana O, Fischetti F, Faganello G, Gatti D, Tarantini L, et al. Cardiovascular risk stratification and management of patients with rheumatoid arthritis in clinical practice: the "EPIDAURO registry." Int J Cardiol. 2014 Mar 15;172(2):534–6.

26. Jagpal A, Navarro-Millán I. Cardiovascular co-morbidity in patients with rheumatoid arthritis: a narrative review of risk factors, cardiovascular risk assessment and treatment. BMC Rheumatol. 2018 Apr 11;2:10.

27. Gabriel SE. Cardiovascular Morbidity and Mortality in Rheumatoid Arthritis. Am J Med. 2008 Oct;121(10 Suppl 1):S9-14.

28. Bhattacharya PK, Barman B, Jamil M, Bora K. Metabolic Syndrome and Atherogenic Indices in Rheumatoid Arthritis and their Relationship with Disease Activity: A Hospital-based Study from Northeast India. J Transl Intern Med. 2020 Jun;8(2):99–105.

29. Krampe SF, Andrade NPB de, Silveira LG da, Brenol CV. Prevalence and Incidence of Metabolic Syndrome in a Cohort of Patients with Rheumatoid Arthritis: A Correlation between Body Mass Index and Disease Activity. Open J Rheumatol Autoimmune Dis. 2020 Jun 9;10(3):95–108.

30. Shaikh S, Dahani A, Arain SR, Khan F. Metabolic Syndrome In Young Rheumatoid Arthritis Patients. J Ayub Med Coll Abbottabad JAMC. 2020 Sep;32(3):318–22.

31. Oliveira BMGB de, Medeiros MM das C, Cerqueira JVM de, Quixadá RT de S, Oliveira ÍMX de. Metabolic syndrome in patients with rheumatoid arthritis followed at a University Hospital in Northeastern Brazil. Rev Bras Reumatol. 2016 Apr;56:117–25.

32. Baker JF, Mehta NN, Baker DG, Toedter G, Shults J, Von Feldt JM, et al. Vitamin D, metabolic dyslipidemia, and metabolic syndrome in rheumatoid arthritis. Am J Med. 2012 Oct;125(10):1036.e9-1036.e15.

33. Montagna GL, Cacciapuoti F, Buono R, Manzella D, Mennillo GA, Arciello A, et al. Insulin resistance is an independent risk factor for atherosclerosis in rheumatoid arthritis. Diab Vasc Dis Res. 2007 Jun 1;4(2):130–5.

34. Rostom S, Mengat M, Lahlou R, Hari A, Bahiri R, Hajjaj-Hassouni N. Metabolic syndrome in rheumatoid arthritis: case control study. BMC Musculoskelet Disord. 2013 Apr 26;14:147.

35. Ross R, Neeland IJ, Yamashita S, Shai I, Seidell J, Magni P, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. Nat Rev Endocrinol. 2020 Mar;16(3):177–89.

36. Guimarães MFB de R, de Andrade MVM, Machado CJ, Vieira ÉLM, Pinto MR da C, Júnior ALT, et al. Leptin as an obesity marker in rheumatoid arthritis. Rheumatol Int. 2018 Sep 1;38(9):1671–7.

37. Francisco V, Ruiz-Fernández C, Pino J, Mera A, González-Gay MA, Gómez R, et al. Adipokines: Linking metabolic syndrome, the immune system, and arthritic diseases. Biochem Pharmacol. 2019 Jul;165:196–206.

38. Dickson BM, Roelofs AJ, Rochford JJ, Wilson HM, De Bari C. The burden of metabolic syndrome on osteoarthritic joints. Arthritis Res Ther. 2019 Dec 16;21(1):289.

39. Apostolopoulos D, Vincent F, Hoi A, Morand E. Associations of metabolic syndrome in SLE. Lupus Sci Med. 2020 Nov 1;7(1):e000436.

40. Theengh DP, Yadav P, Jain AK, Nandy P. Assessment of metabolic syndrome in HIV-infected individuals. Indian J Sex Transm Dis AIDS. 2017;38(2):152–6.

41. Santo RCE, Fernandes KZ, Lora PS, Filippin LI, Xavier RM. Prevalence of rheumatoid cachexia in rheumatoid arthritis: a systematic review and meta-analysis. J Cachexia Sarcopenia Muscle. 2018 Oct;9(5):816–25.

42. Torii M, Hashimoto M, Hanai A, Fujii T, Furu M, Ito H, et al. Prevalence and factors associated with sarcopenia in patients with rheumatoid arthritis. Mod Rheumatol. 2019 Jul;29(4):589–95.

43. Yan M, Zhang J, Yang H, Sun Y. The role of leptin in osteoarthritis. Medicine (Baltimore). 2018 Apr 6;97(14):e0257.

44. Oyoo GO, Ogola EN, Kirui F, Amayo EO. Cardiovascular risk factors in patients with rheumatoid arthritis at Kenyatta National Hospital, Nairobi Kenya. 2013 [cited 2021 Oct 8]; Available from: http://erepository.uonbi.ac.ke/handle/11295/34536

45. Hamamoto K, Yamada S, Yasumoto M, Yoda M, Yoda K, Tsuda A, et al. Association of Nocturnal Hypertension With Disease Activity in Rheumatoid Arthritis. Am J Hypertens. 2016 Mar;29(3):340–7.

46. Panoulas VF, Metsios GS, Pace AV, John H, Treharne GJ, Banks MJ, et al. Hypertension in rheumatoid arthritis. Rheumatology. 2008 Sep 1;47(9):1286–98.

47. Agca R, Hopman LHGA, Laan KJC, van Halm VP, Peters MJL, Smulders YM, et al. Cardiovascular Event Risk in Rheumatoid Arthritis Compared with Type 2 Diabetes: A 15-year Longitudinal Study. J Rheumatol. 2020 Mar;47(3):316–24.

48. Lu MC, Yan ST, Yin WY, Koo M, Lai NS. Risk of Rheumatoid Arthritis in Patients with Type 2 Diabetes: A Nationwide Population-Based Case-Control Study. PLOS ONE. 2014 Jul 2;9(7):e101528.

49. Baghdadi LR. Effect of methotrexate use on the development of type 2 diabetes in rheumatoid arthritis patients: A systematic review and meta-analysis. PLOS ONE. 2020 Jul 6;15(7):e0235637.

50. Nicolau J, Lequerré T, Bacquet H, Vittecoq O. Rheumatoid arthritis, insulin resistance, and diabetes. Joint Bone Spine. 2017 Jul 1;84(4):411–6.

51. Dong Q, Liu H, Yang D, Zhang Y. Diabetes mellitus and arthritis: is it a risk factor or comorbidity?: A systematic review and meta-analysis. Medicine (Baltimore). 2017 May;96(18):e6627.

52. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The Impact of Traditional Cardiovascular Risk Factors on Cardiovascular Outcomes in Patients with Rheumatoid Arthritis: A Systematic Review and Meta-Analysis. PLOS ONE. 2015 Feb 17;10(2):e0117952.

53. Kerola AM, Rollefstad S, Semb AG. Atherosclerotic Cardiovascular Disease in Rheumatoid Arthritis: Impact of Inflammation and Antirheumatic Treatment. Eur Cardiol Rev. 2021 May 13;16:e18.

54. Semb AG, Ikdahl E, Kerola AM, Wibetoe G, Sexton J, Crowson CS, et al. A Clinical Audit of Cardiovascular Risk Factors and Disease in Patients with Rheumatoid Arthritis - SURF-RA. Mediterr J Rheumatol. 2022 Jun;33(2):201–17.

55. Ambrosino P, Lupoli R, Di Minno A, Tasso M, Peluso R, Di Minno MND. Subclinical atherosclerosis in patients with rheumatoid arthritis. A meta-analysis of literature studies. Thromb Haemost. 2015 May;113(5):916–30.

56. Goff DC, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, et al. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. Circulation. 2014 Jun 24;129(25_suppl_2):S49–73.

57. Weber B, Weisenfeld D, Seyok T, Huang S, Massarotti E, Barrett L, et al. Relationship Between Risk of Atherosclerotic Cardiovascular Disease, Inflammation, and Coronary Microvascular Dysfunction in Rheumatoid Arthritis. J Am Heart Assoc. 2022 Jun 7;11(11):e025467.

58. Fransen J, Stucki G, van Riel PLCM. Rheumatoid arthritis measures: Disease Activity Score (DAS), Disease Activity Score-28 (DAS28), Rapid Assessment of Disease Activity in Rheumatology (RADAR), and Rheumatoid Arthritis Disease Activity Index (RADAI). Arthritis Care Res. 2003;49(S5):S214–24.

59. Fransen J, Langenegger T, Michel BA, Stucki G, for the members of the Swiss Clinical Quality Management in Rheumatoid Arthritis. Feasibility and validity of the RADAI, a self-administered rheumatoid arthritis disease activity index. Rheumatology. 2000 Mar 1;39(3):321–7.

60. ANDERSON J, CAPLAN L, YAZDANY J, ROBBINS ML, NEOGI T, MICHAUD K, et al. Rheumatoid Arthritis Disease Activity Measures: American College of Rheumatology Recommendations for Use in Clinical Practice. Arthritis Care Res. 2012 May;64(5):640–7.

61. England BR, Tiong BK, Bergman MJ, Curtis JR, Kazi S, Mikuls TR, et al. 2019 Update of the American College of Rheumatology Recommended Rheumatoid Arthritis Disease Activity Measures. Arthritis Care Res. 2019 Dec;71(12):1540–55.

62. van Riel PLCM, Renskers L. The Disease Activity Score (DAS) and the Disease Activity Score using 28 joint counts (DAS28) in the management of rheumatoid arthritis. Clin Exp Rheumatol. 2016 Oct;34(5 Suppl 101):S40–4.

63. Cui K, Movahedi M, Bombardier C, Kuriya B. Cardiovascular risk factors are negatively associated with rheumatoid arthritis disease outcomes. Ther Adv Musculoskelet Dis. 2021;13:1759720X20981217.

64. Azevedo S, Santos-Faria D, Leite Silva J, Ramos Rodrigues J, Sousa Neves J, Peixoto D, et al. Obesity, metabolic syndrome and other comorbidities in rheumatoid arthritis and psoriatic arthritis: influence on disease activity and quality of life. Acta Reumatol Port. 2019 Dec;44(4):322–4.

65. DAS 28 - Disease Activity Score Calculator for Rheumatoid Arthritis [Internet]. [cited 2021 Sep 17]. Available from: http://www.4s-dawn.com/DAS28/

66. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. Gastroenterol Hepatol Bed Bench. 2013;6(1):14–7.

67. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2010 Sep 1;69(9):1580–8.

68. Flack JM, Adekola B. Blood pressure and the new ACC/AHA hypertension guidelines. Trends Cardiovasc Med. 2020 Apr 1;30(3):160–4.

69. Association AD. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care. 2021 Jan 1;44(Supplement 1):S15–33.

70. CDC. All About Adult BMI [Internet]. Centers for Disease Control and Prevention. 2021 [cited 2021 Sep 17]. Available from: https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html

71. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and Management of the Metabolic Syndrome. Circulation. 2005 Oct 25;112(17):e285–90.

72. Erum U, Ahsan T, Khowaja D. Lipid abnormalities in patients with Rheumatoid Arthritis. Pak J Med Sci. 2017;33(1):227–30.

73. Gamal SM, Eleishi HH, Moghazy A, El-Garf K, Eissa M, Sobhy N, et al. Effect of education on disease activity and functional status in rheumatoid arthritis patients. Egypt Rheumatol. 2021 Jan 1;43(1):7–11.

74. Gomez D, Saavedra-Martinez G, Villarreal L, Santos-Moreno P, Bello-Gualtero J, Giraldo V, et al. SAT0108 Misdiagnosis of Rheumatoid Arthritis – The Photography. Ann Rheum Dis. 2015 Jun 1;74(Suppl 2):689–689.

75. Thompson AE, Anisimowicz Y, Miedema B, Hogg W, Wodchis WP, Aubrey-Bassler K. The influence of gender and other patient characteristics on health care-seeking behaviour: a QUALICOPC study. BMC Fam Pract. 2016 Mar 31;17:38.

76. Zhu J, Niu Z, Alfredsson L, Klareskog L, Padyukov L, Jiang X. Age at menarche, age at natural menopause, and risk of rheumatoid arthritis — a Mendelian randomization study. Arthritis Res Ther. 2021;23:108.

77. Kvien TK, Uhlig T, Ødegård S, Heiberg MS. Epidemiological aspects of rheumatoid arthritis: the sex ratio. Ann N Y Acad Sci. 2006 Jun;1069:212–22.

78. Stack RJ, Nightingale P, Jinks C, Shaw K, Herron-Marx S, Horne R, et al. Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK: an observational study. BMJ Open. 2019 Mar 4;9(3):e024361.

79. Innala L, Berglin E, Möller B, Ljung L, Smedby T, Södergren A, et al. Age at onset determines severity and choice of treatment in early rheumatoid arthritis: a prospective study. Arthritis Res Ther. 2014 Apr 14;16(2):R94.

80. Jiang X, Sandberg MEC, Saevarsdottir S, Klareskog L, Alfredsson L, Bengtsson C. Higher education is associated with a better rheumatoid arthritis outcome concerning for pain and function but not disease activity: results from the EIRA cohort and Swedish rheumatology register. Arthritis Res Ther. 2015;17:317.

81. Molina E, Del Rincon I, Restrepo JF, Battafarano DF, Escalante A. Association of socioeconomic status with treatment delays, disease activity, joint damage, and disability in rheumatoid arthritis. Arthritis Care Res. 2015 Jul;67(7):940–6.

82. Pincus T, Callahan LF. Formal education as a marker for increased mortality and morbidity in rheumatoid arthritis. J Chronic Dis. 1985;38(12):973–84.

83. Cai W, Tang X, Pang M. Prevalence of Metabolic Syndrome in Patients With Rheumatoid Arthritis: An Updated Systematic Review and Meta-Analysis. Front Med [Internet]. 2022 [cited 2023 Jan 2];9. Available from: https://www.frontiersin.org/articles/10.3389/fmed.2022.855141

84. COJOCARU M, COJOCARU IM, SILOSI I, VRABIE CD. Metabolic Syndrome in Rheumatoid Arthritis. Mædica. 2012 Jun;7(2):148–52.

85. Karvounaris SA, Sidiropoulos PI, Papadakis JA, Spanakis EK, Bertsias GK, Kritikos HD, et al. Metabolic syndrome is common among middle-to-older aged Mediterranean patients with rheumatoid arthritis and correlates with disease activity: a retrospective, cross-sectional, controlled, study. Ann Rheum Dis. 2007 Jan 1;66(1):28–33.

86. Šalamon L, Morović-Vergles J, Marasović-Krstulović D, Kehler T, Šakić D, Badovinac O, et al. Differences in the prevalence and characteristics of metabolic syndrome in rheumatoid arthritis and osteoarthritis: a multicentric study. Rheumatol Int. 2015 Dec;35(12):2047–57.

87. Elkan AC, Håkansson N, Frostegård J, Cederholm T, Hafström I. Rheumatoid cachexia is associated with dyslipidemia and low levels of atheroprotective natural antibodies against phosphorylcholine but not with dietary fat in patients with rheumatoid arthritis: a cross-sectional study. Arthritis Res Ther. 2009 Mar 10;11(2):R37.

88. Katz PP, Yazdany J, Trupin L, Schmajuk G, Margaretten M, Barton J, et al. Sex differences in assessment of obesity in rheumatoid arthritis. Arthritis Care Res. 2013 Jan;65(1):62–70.

89. Dessein PH, Woodiwiss AJ, Norton GR, Solomon A. Rheumatoid arthritis is associated with reduced adiposity but not with unfavorable major cardiovascular risk factor profiles and enhanced carotid atherosclerosis in black Africans from a developing population: a cross-sectional study. Arthritis Res Ther. 2013 Aug 22;15(4):R96.

90. Manavathongchai S, Bian A, Rho YH, Oeser A, Solus JF, Gebretsadik T, et al. Inflammation and Hypertension in Rheumatoid Arthritis. J Rheumatol. 2013 Nov 1;40(11):1806–11.

91. Al-Ahmari AK. Prevalence of Hypertension and Its Associated Risk Factors Among Patients with Rheumatoid Arthritis in the Kingdom of Saudi Arabia. Int J Gen Med. 2022 Aug 8;15:6507–17.

92. Cypienė A, Dadonienė J, Rugienė R, Ryliškytė L, Kovaitė M, Petrulionienė Z, et al. The influence of mean blood pressure on arterial stiffening and endothelial dysfunction in women with rheumatoid arthritis and systemic lupus erythematosus. Med Kaunas Lith. 2010;46(8):522–30.

93. Roman MJ, Devereux RB, Schwartz JE, Lockshin MD, Paget SA, Davis A, et al. Arterial stiffness in chronic inflammatory diseases. Hypertens Dallas Tex 1979. 2005 Jul;46(1):194–9.

94. Hadwen B, Stranges S, Barra L. Risk factors for hypertension in rheumatoid arthritis patients–A systematic review. Autoimmun Rev. 2021 Apr 1;20(4):102786.

95. Ursini F, Russo E, D'Angelo S, Arturi F, Hribal ML, D'Antona L, et al. Prevalence of Undiagnosed Diabetes in Rheumatoid Arthritis: an OGTT Study. Medicine (Baltimore). 2016 Feb;95(7):e2552.

96. Semb AG, Rollefstad S, Ikdahl E, Wibetoe G, Sexton J, Crowson C, et al. Diabetes mellitus and cardiovascular risk management in patients with rheumatoid arthritis: an international audit. RMD Open. 2021 Jul 1;7(2):e001724.

97. Verma AK, Bhatt D, Goyal Y, Dev K, Beg MMA, Alsahli MA, et al. Association of Rheumatoid Arthritis with Diabetic Comorbidity: Correlating Accelerated Insulin Resistance to Inflammatory Responses in Patients . J Multidiscip Healthc. 2021 Apr 12;14:809–20.

98. Tian Z, Mclaughlin J, Verma A, Chinoy H, Heald AH. The relationship between rheumatoid arthritis and diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Endocrinol Metab. 2021 Feb 19;10(2):125–31.

99. Akiyama M, Mawatari T, Nakashima Y, Miyahara H, Yamada H, Okazaki K, et al. Prevalence of dyslipidemia in Japanese patients with rheumatoid arthritis and effects of atorvastatin treatment. Clin Rheumatol. 2015 Nov;34(11):1867–75.

100. Boers M, Nurmohamed MT, Doelman CJA, Lard LR, Verhoeven AC, Voskuyl AE, et al. Influence of glucocorticoids and disease activity on total and high density lipoprotein cholesterol in patients with rheumatoid arthritis. Ann Rheum Dis. 2003 Sep 1;62(9):842–5.

101. Hadda V, Handa R, Aggarwal P, Lakshmy R, Kumar U, Pandey R. Disease activity and lipids in rheumatoid arthritis: a prospective study. Indian J Rheumatol. 2007 Dec 1;2(4):137–40.

102. Montiel de Jarolín DE, Holtzberger S, Gill C. Frequency of dyslipidemia and other cardiovascular risk factors in patients with rheumatoid arthritis. Rev Nac Itauguá. 2018 Dec;10(2):93–104.

103. Mena-Vázquez N, Redondo-Rodríguez R, Rioja J, Jimenez-Nuñez FG, Manrique-Arija S, Lisbona-Montañez JM, et al. Postprandial Hyperlipidemia: Association with Inflammation and Subclinical Atherosclerosis in Patients with Rheumatoid Arthritis. Biomedicines. 2022 Jan;10(1):133.

104. Bag-Ozbek A, Giles JT. Inflammation, adiposity, and atherogenic dyslipidemia in rheumatoid arthritis: is there a paradoxical relationship? Curr Allergy Asthma Rep. 2015 Feb;15(2):497.

105. García-Gómez C, Nolla JM, Valverde J, Narváez J, Corbella E, Pintó X. High HDL-cholesterol in women with rheumatoid arthritis on low-dose glucocorticoid therapy. Eur J Clin Invest. 2008 Sep;38(9):686–92.

106. Salaffi F, Carotti M, Di Carlo M, Tardella M, Lato V, Becciolini A, et al. The Expanded Risk Score in Rheumatoid Arthritis (ERS-RA): performance of a disease-specific calculator in comparison with the traditional prediction scores in the assessment of the 10-year risk of cardiovascular disease in patients with rheumatoid arthrit. Swiss Med Wkly. 2018 Aug 13;148:w14656.

107. Gerasimova EV, Popkova TV, Gerasimova DA, Glukhova SI, Nasonov EL, Lila AM. [Application of cardiovascular risk scales to identify carotid atherosclerosis in patients with rheumatoid arthritis]. Ter Arkh. 2021 May 15;93(5):561–7.

108. Kim SH, Lee SH, Kim HR, Min HK. Cardiovascular disease risk calculators to reflect the subclinical atherosclerosis of coronary artery in rheumatoid arthritis: a pilot study. BMC Rheumatol. 2021 Aug 30;5(1):39.

109. Wah-Suarez MI, Galarza-Delgado DA, Azpiri-Lopez JR, Colunga-Pedraza IJ, Cardenas-de la Garza JA, Vera-Pineda R, et al. The best cardiovascular risk calculator to predict carotid plaques in rheumatoid arthritis patients. Clin Rheumatol. 2018 Sep;37(9):2373–80.

110. Intriago M, Maldonado G, Cárdenas J, Ríos C. Clinical Characteristics in Patients with Rheumatoid Arthritis: Differences between Genders. Sci World J. 2019 Jul 3;2019:e8103812.

111. Sokka T, Toloza S, Cutolo M, Kautiainen H, Makinen H, Gogus F, et al. Women, men, and rheumatoid arthritis: analyses of disease activity, disease characteristics, and treatments in the QUEST-RA Study. Arthritis Res Ther. 2009 Jan 14;11(1):R7.

112. Hutchinson D, Shepstone L, Moots R, Lear JT, Lynch MP. Heavy cigarette smoking is strongly associated with rheumatoid arthritis (RA), particularly in patients without a family history of RA. Ann Rheum Dis. 2001 Mar 1;60(3):223–7.

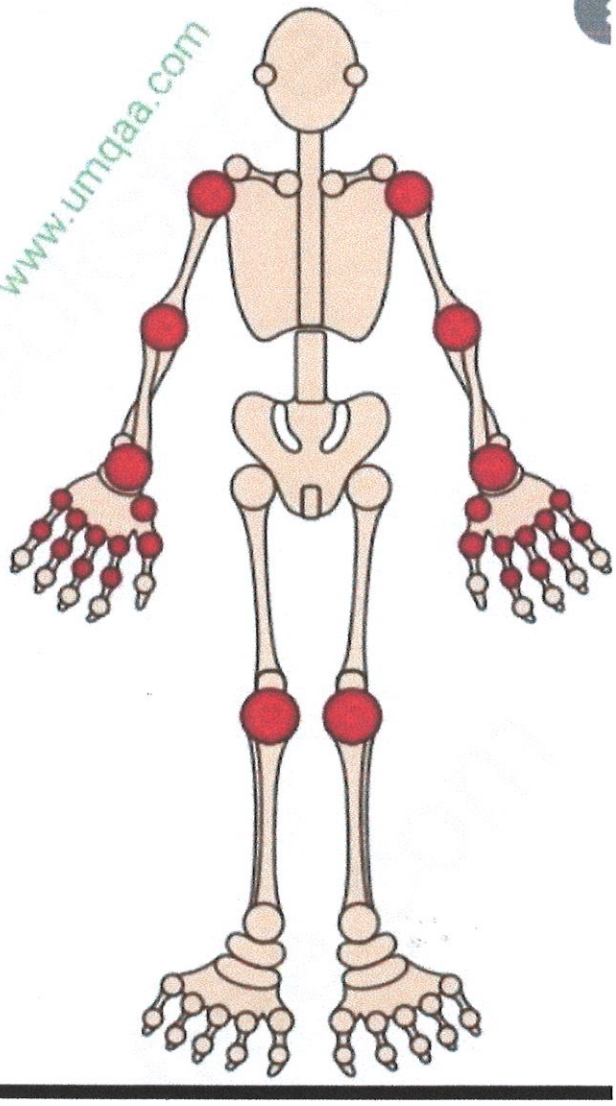
113. Saag KG, Cerhan JR, Kolluri S, Ohashi K, Hunninghake GW, Schwartz DA. Cigarette smoking and rheumatoid arthritis severity. Ann Rheum Dis. 1997 Aug;56(8):463–9.

114. Jiang N, Li Q, Li H, Fang Y, Wu L, Duan X, et al. Chinese registry of rheumatoid arthritis (CREDIT) V: sex impacts rheumatoid arthritis in Chinese patients. Chin Med J (Engl). 2022 Sep 20;135(18):2210.

7. Appendix

7.1 DASS-28 Scoring Chart

Disease activity	DAS28 value
Remission	DAS28 ≤ 2.6
Low disease activity	2.6 < DAS28 ≤ 3.2
Moderate disease activity	3.2 < DAS28 ≤ 5.1
High disease activity	5.1 < DAS28



7.2 Patient's Data Entry Form

Patient No.							
Current Age		Sex		Age at Diagnosis		Disease Duration	
Level of Education		Waist circumference		CRP		ESR	
BP		RBS		FBS		HbA1C	
Prescribed Medications							
Patient's weight (Kg)		Patient's Height		BMI		Smoking	
DAS28 Score		Total Cholesterol		HDL-C Levels		TG Levels	
History of stroke/MI		10-year CVD score					

7.3 Subject Information and Consent Form

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PARTICIPANT INFORMATION AND CONSENT FORMSAMPLE ADULT CONSENT

FOR ENROLLMENT IN THE STUDY

(To be administered in English or any other appropriate language e.g Kiswahili translation)

Title of Study: METABOLIC SYNDROME IN RHEUMATOID ARTHRTIS PATIENTS: PREVALNCE AND RISK FACTORS

Principal Investigator\and institutional affiliation: JEREMIAH MUNGUTI, UNIVERSITY OF NAIROBI

Co-Investigator and institutional affiliation: PROF OMONDI OYOO, UNIVERSITY OF NAIROBI

Co-Investigator and institutional affiliation: PROF ELIJAH OGOLA, UNIVERSITY OF NAIROBI

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will requestyou to sign your name on this form. You should understand the general principles which apply to all participants in a medical research: (i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal (iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and

Research Committee protocol No. _____

WHAT IS THIS STUDY ABOUT?

This study is about metabolic syndrome in patients with a disease called rheumatoid arthritis. This is a disease that mainly affects joints. Untreated, the disease can badly affect the patient's wellbeing and overall quality of life. Relative to the general population, patients with rheumatoid arthritis have an increased risk of developing other diseases including obesity, high blood pressure, diabetes and increase of unhealthy fats in their blood. When all these conditions occur together in the same person, the affected patient is said to have metabolic syndrome, a condition that makes affected patients have a higher risk of stroke and heart failure compared to the general population. The number of patients with rheumatoid arthritis who have metabolic syndrome has been reported to differ from one population to another. Known contributors to metabolic syndrome in rheumatoid arthritis include a longer duration of having the disease, having a more severe disease, the patient's lifestyle, and the effect of medicines taken by the patient on their general health. How these factors contribute to the development of metabolic syndrome in patients with rheumatoid arthritis has however, been shown to vary in different populations. Hardly any local studies have attempted to determine the association of these contributors of metabolic syndrome and rheumatoid arthritis. This is despite the different socioeconomic and demographic factors that limit patients' access to quality healthcare in our local setup.

The researchers listed above are interviewing individuals who are adult Kenyans. The purpose of the interview is to find out whether they consent to the use of information from their medical records and to have certain measurements taken including their blood pressure, height, weight and abdominal circumference. Participants will not undergo any further medical tests.

There will be approximately 89 participants in this study who will be chosen randomly. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen: You will be interviewed by a trained interviewer in a private area (a separate consultation room) where you feel comfortable answering questions. The interview will last approximately 20 minutes (maximum of 30 minutes) and will include taking the following measurements: blood pressure, weight, height and abdominal circumference.

After the interview has finished, we will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. The reasons why we may need to contact you include: Medical re-evaluation if from the measurements taken and the records from your file, it is noted that you are at an increased risk of stroke or heart disease and no appropriate measures have been taken to reduce this risk.

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. One potential risk of being in this study is loss of privacy. We will keep everything you tell us as confidential as possible. We will also use a code number to identify you in a password-protected computer database and we will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions that you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview. Furthermore, all study staff and interviewers are professionals with special training in these examinations/interviews.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

You may benefit by receiving free counselling on reducing your risk of having metabolic syndrome and thus a higher risk of stroke or heart disease. We will refer you to a qualified specialist for care and support where necessary. Also, the information you provide will help us better understand the burden of metabolic syndrome in patients with rheumatoid arthritis. This information is a contribution to science and will help in defining the burden of stroke and heart disease risk in patients with rheumatoid arthritis

WILL BEING IN THIS STUDY COST YOU ANYTHING?

No additional cost will be incurred by choosing to participate in this study

WILL YOU GET REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

No refund will be given for participants since no additional cost to their care will be incurred.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have also had the chance to discuss this research study with the Principal Investigator. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identityconfidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participantin a research study.

I agree to participate in this research study:	**Yes**	**No**
I agree to provide contact information for follow-up:	Yes	No

Participant printed name: _____

Participant signature / Thumb stamp_____

Date _____

Witness Signature/_____

Date:_____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participantnamed above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name: JEREMIAH MUNGUTI

Date: 07/01/2022 **Signature** _____

Role in the study: PRINCIPAL INVESTIGATOR

For more information contact JEREMIAH MUNGUTI at 0735985085 from 8 am to 5 pm

Witness Name_____ Signature /Thumb stamp: _____
Contact information _____ **Date;** _____

7.4 Taarifa ya Somo na Fomu ya Idhini

MAELEZO YA MSHIRIKI NA FOMU YA RIDHAA YA MFANO WA RIDHAA YA MTU MZIMA KWA KUJIANDIKISHA KATIKA MAFUNZO

(Itasimamiwa kwa Kiingereza au lugha nyingine yoyote inayofaa k.m tafsiri ya Kiswahili)

Kichwa cha Utafiti: UGONJWA WA UMETABOLI KATIKA WAGONJWA WA BARIDI YABISI: UENEAJI NA MAMBO HATARI

Mchunguzi Mkuu\na uhusiano wa kitaasisi: JEREMIAH MUNGUTI, CHUO KIKUU CHA NAIROBI.

Mchunguzi-Mwenza na uhusiano wa kitaasisi: PROF OMONDI OYOO, CHUO KIKUU CHA NAIROBI

Mchunguzi-Mwenza na uhusiano wa kitaasisi: PROF ELIJAH OGOLA, CHUO KIKUU CHA NAIROBI

Utangulizi: Ningependa kukuambia kuhusu utafiti unaofanywa na watafiti walioorodheshwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa taarifa utakayohitaji ili kukusaidia kuamua kama kuwa mshiriki au la katika utafiti huu. Jisikie huru kuuliza maswali yoyote kuhusu madhumuni ya utafiti, nini kitatokea ukishiriki katika utafiti, hatari na manufaa yanayoweza kutokea, haki zako kama mtu wa kujitolea, na jambo lingine lolote kuhusu utafiti au fomu hii ambalo haliko wazi. Wakati tumejibu maswali yako yote kwa kuridhika kwako, unaweza kuamua kuwa katika utafiti au la. Utaratibu huu unaitwa 'kibali cha taarifa'. Ukishaelewa na kukubali kuwa katika utafiti, nitakuomba utie sahihi jina lako kwenye fomu hii. Unapaswa kuelewa kanuni za jumla zinazotumika kwa washiriki wote katika utafiti wa kimatibabu: (i) Uamuzi wako wa kushiriki ni wa hiari kabisa ii) Unaweza kujiondoa kwenye utafiti wakati wowote bila ya kuhitaji kutoa sababu ya kujiondoa (iii) Kukataa. kushiriki katika utafiti hakutaathiri huduma unazostahiki katika kituo hiki cha afya au vituo vingine. Tutakupa nakala ya fomu hii kwa rekodi zako.

Naweza kuendelea? NDIO /LA

Utafiti huu umeidhinishwa na Itifaki ya Kamati ya Maadili na Utafiti ya Hospitali ya Kitaifa ya Kenyatta-Chuo Kikuu cha Nairobi Nambari_____.

UTAFITI HUU UNAHUSU NINI?

Utafiti huu unahusu kuenea kwa ugonjwa wa kimetaboliki kwa wagonjwa walio na baridi yabisis (aina ya ugonjwa wa viungo). Baridi yabisi ni ugonjwa unaoathiri hasa viungo. Bila kutibiwa, ugonjwa unaweza kuathiri vibaya ustawi wa mgonjwa na ubora wa maisha kwa ujumla. Ikilinganishwa na idadi ya watu kwa ujumla, wagonjwa wenye baridi yabisi wana hatari kubwa ya kupata magonjwa mengine ikiwa ni pamoja na uongezeko wa uzani wa mwili, shinikizo la damu, kisukari na ongezeko la mafuta yasiyo ya afya katika damu yao. Hali hizi zote zinapotokea kwa pamoja katika mtu mmoja, mgonjwa aliyeathiriwa anasemekana kuwa na ugonjwa wa kimetaboliki, hali ambayo inawaweka hatarini zaidi ya kiharusi (stroke) na kushindwa kwa moyo ikilinganishwa na idadi ya watu kwa ujumla. Idadi ya wagonjwa walio na ugonjwa wa baridi yabisi ambao wana ugonjwa wa kimetaboliki imeripotiwa kutofautiana kutoka idadi moja hadi nyingine. Wachangiaji wanaojulikana wa ugonjwa wa kimetaboliki

katika arthritis ya rheumatoid ni pamoja na muda na ukali wa ugonjwa huo, mtindo wa maisha wa mgonjwa, na athari za dawa zilizoagizwa kwa afya ya wagonjwa kwa ujumla. Jinsi mambo haya yanavyochangia katika ukuzaji wa ugonjwa wa kimetaboliki katika ugonjwa wa baridi yabisi, hata hivyo, imeonyeshwa kutofautiana katika tafiti tofauti na karibu hakuna tafiti za kienyeji zimejaribu kubaini uhusiano wao katika ugonjwa wa baridi yabisi. Hii ni licha ya sababu tofauti za kijamii na kiuchumi na idadi ya watu zinazozuia ufikiaji wa wagonjwa kwa huduma bora za afya katika usanidi wetu wa karibu.

Watafiti walioorodheshwa hapo juu wanawahoji watu ambao ni Wakenya watu wazima. Madhumuni ya mahojiano ni kujua kama wanakubali matumizi ya taarifa kutoka kwenye rekodi zao za matibabu na kuchukuliwa vipimo fulani ikiwa ni pamoja na shinikizo la damu, urefu, uzito na mzunguko wa tumbo. Washiriki hawatapitia vipimo vingine vya matibabu.

Kutakuwa na takriban washiriki 89 katika utafiti huu ambao watachaguliwa bila mpangilio. Tunaomba idhini yako ili kuzingatia kushiriki katika utafiti huu.

NINI KITAENDELEA UKIAMUA KUWA KATIKA UTAFITI HUU?

Ukikubali kushiriki katika utafiti huu, mambo yafuatayo yatafanyika: Utahojiwa na mhoji aliyefunzwa katika eneo la faragha ambapo unahisi kujibu maswali. Mahojiano yatachukua takriban dakika 20 na yatajumuisha kuchukua vipimo vifuatavyo: shinikizo la damu, uzito, urefu na mduara wa tumbo.

Baada ya mahojiano kukamilika, tutaomba nambari ya simu ambapo tunaweza kuwasiliana nawe ikibidi. Ukikubali kutoa maelezo yako ya mawasiliano, yatatumiwa na watu wanaofanya kazi katika utafiti huu pekee na kamwe hayatashirikiwa na wengine. Sababu ambazo tunaweza kuhitaji kuwasiliana nawe ni pamoja na: Tathmini upya ya matibabu ikiwa kutoka kwa vipimo vilivyochukuliwa na rekodi kutoka kwa faili yako, imebainika kuwa uko kwenye hatari kubwa ya kiharusi au ugonjwa wa moyo na hakuna hatua zinazofaa zimechukuliwa ili kupunguza hatari hii.

JE, KUNA HATARI, MADHARA YOYOTE YANAYOHUSISHWA NA UTAFITI HUU?

Utafiti wa kimatibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihisia na kimwili. Hatari moja inayoweza kutokea ya kuwa katika utafiti huu ni kupoteza faragha. Tutaweka kila kitu unachotuambia kama siri iwezekanavyo. Pia tutatumia nambari ya msimbo kukutambua katika hifadhidata ya kompyuta iliyolindwa na nenosiri na tutaweka rekodi zetu zote za karatasi kwenye kabati ya faili iliyofungwa. Hata hivyo, hakuna mfumo wa kulinda usiri wako unaoweza kuwa salama kabisa, kwa hivyo bado kuna uwezekano kwamba mtu anaweza kujua ulikuwa kwenye utafiti huu na kupata taarifa kukuhusu.

Pia, kujibu maswali katika mahojiano kunaweza kuwa na wasiwasi kwako. Ikiwa kuna maswali yoyote ambayo hutaki kujibu, unaweza kuyaruka. Una haki ya kukataa mahojiano au maswali yoyote yaliyoulizwa wakati wa mahojiano. Zaidi ya hayo, wafanyakazi wote wa utafiti na wahojaji ni wataalamu walio na mafunzo maalum katika mitihani/mahojiano haya.

JE, KUNA FAIDA YOYOTE KUWA KATIKA UTAFITI HUU?

Unaweza kufaidika kwa kupokea ushauri wa bure juu ya kupunguza hatari yako ya kuwa na ugonjwa wa kimetaboliki na hivyo hatari kubwa ya kiharusi au ugonjwa wa moyo. Tutakuelekeza kwa mtaalamu aliyehitimu kwa matunzo na usaidizi inapobidi. Pia, maelezo

utakayotoa yatatusaidia kuelewa vyema mzigo wa ugonjwa wa kimetaboliki kwa wagonjwa walio na baridi yabisi. Habari hii ni mchango kwa sayansi na itasaidia katika kufafanua mzigo wa kiharusi na hatari ya ugonjwa wa moyo kwa wagonjwa wa baridi yabisi.

JE, KUWA KATIKA SOMO HILI ITAKUGHARIMU LOLOTE?
Hakuna gharama ya ziada itakayotozwa kwa kuchagua kushiriki katika utafiti huu

JE, UTAREJESHWA KWA FEDHA ZOZOTE ULIZOTUMIA SEHEMU YA UTAFITI HUU?
Hakuna kurejeshewa pesa kwa washiriki kwa kuwa hakuna gharama ya ziada kwa utunzaji wao itatozwa.

VIPI IKIWA UNA MASWALI BAADAYE?
Ikiwa una maswali zaidi au wasiwasi kuhusu kushiriki katika utafiti huu, tafadhali piga simu au tuma ujumbe mfupi wa maandishi kwa wafanyikazi wa utafiti kupitia nambari iliyotolewa chini ya ukurasa huu.

Kwa maelezo zaidi kuhusu haki zako kama mshiriki wa utafiti unaweza kuwasiliana na Katibu/Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Kamati ya Maadili na Utafiti ya Chuo Kikuu cha Nairobi Nambari 2726300 Ext. 44102 barua pepe uonknh_erc@uonbi.ac.ke.
Wafanyikazi wa utafiti watakurudishia malipo yako kwa nambari hizi ikiwa simu ni ya mawasiliano yanayohusiana na masomo.

UCHAGUZI WAKO MENGINE NI GANI?
Uamuzi wako wa kushiriki katika utafiti ni wa hiari. Uko huru kukataa kushiriki katika utafiti na unaweza kujiondoa kwenye utafiti wakati wowote bila dhuluma au hasara ya manufaa yoyote.

FOMU YA RIDHAA (TAARIFA YA RIDHAA)
Kauli ya mshiriki:
Nimesoma fomu hii ya idhini au nimesomewa maelezo. Pia nimepata nafasi ya kujadili utafiti huu na Mpelelezi Mkuu. Nimejibiwa maswali yangu kwa lugha ninayoielewa. Hatari na faida zimeelezewa kwangu. Ninaelewa kuwa ushiriki wangu katika utafiti huu ni wa hiari na kwamba ninaweza kuchagua kujiondoa wakati wowote. Ninakubali kwa uhuru kushiriki katika utafiti huu wa utafiti.
Ninaelewa kuwa juhudi zote zitafanywa ili kuweka taarifa kuhusu utambulisho wangu wa kibinafsi kuwa siri.

Kwa kutia saini fomu hii ya idhini, sijaacha haki zozote za kisheria nilizo nazo kama mshiriki katika utafiti wa utafiti.

Ninakubali kushiriki katika utafiti huu: Ndiyo/ Hapana
Ninakubali kutoa maelezo ya mawasiliano kwa ufuatiliaji: Ndiyo/ Hapana

Kauli ya mtafiti:
Mimi, niliyetia sahihi chini, nimeeleza kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki aliyetajwa hapo juu na ninaamini kuwa mshiriki ameelewa na ametoa ridhaa yake kwa hiari na kwa uhuru.

Jina la Mtafiti: JEREMIA MUNGUTI
Tarehe: _____ Sahihi_____
Jukumu katika utafiti: UPELELEZI MKUU

Kwa maelezo zaidi wasiliana na JEREMIA MUNGUTI kwa 0735985085 kutoka 8 asubuhi hadi 5 jioni

Jina la Shahidi _____
Sahihi /Muhuri wa kidole gumba: _____ Tarehe:_____
Maelezo ya mawasiliano _____

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This dissertation has been approved for submission by the lead supervisor and the Chairman of the Department of Clininal Medicine and Therapeutics

Signature _____ Date: 7/11/2023

Prof George Omondi Oyoo, Associate Professor (MBChB, MMED (Internal Medicine), FCP (ECSA), FRCP (Edin), FACR)

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Signature _____ Date: 9/11/2023

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