CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS AT KENYATTA NATIONAL HOSPITAL

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A Thesis submitted in partial fulfillment for the award of the degree of Master of Medicine (Internal medicine) at The University of Nairobi.

2009
DECLARATION

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

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This thesis is dedicated to my dear wife Caroline for her patience and humility; to our son Brandon and daughter Brianna; to my late dad for his mentorship; and to my mother from whom I got the strength and motivation to reach this height.
ACKNOWLEDGEMENTS

I would like to express my sincere appreciation and gratitude to the following individuals and organizations:

My supervisors, Dr omondi Oyoo, Professor Ogola and Professor Amayo, who took time off their busy schedules, to guide me in all aspects regarding this work.

- University of Nairobi for giving me the opportunity to do my work at the University.
- Most sincerely many thanks to the Nursing staff at the medical out patient clinics at Kenyatta National Hospital
- My sincere gratitude to Juliet, Karen, Nahashon support in data collection, laboratory work and data analysis.
- The clients who participated in the study.
- Many people not mentioned here and helped in my work in one way or the other; please accept my appreciation and God bless you all
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<td>Cardiovascular disease</td>
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<td>KNH</td>
<td>Kenyatta National Hospital</td>
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<td>RA</td>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Int med</td>
<td>Internal medicine</td>
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<td>M.MED</td>
<td>Master of medicine</td>
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<tr>
<td>Bp</td>
<td>Blood pressure</td>
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<td>NSAID</td>
<td>Non steroidal anti inflammatory drugs</td>
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<td>DMARDS</td>
<td>Disease modifying anti Rheumatic drugs</td>
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<td>MI</td>
<td>Myocardial Infarction</td>
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<td>SPSS</td>
<td>Statistical package for social sciences</td>
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<td>MS ACCESS</td>
<td>Microsoft access</td>
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<td>W.H.O</td>
<td>World Health Organization</td>
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<td>ACR</td>
<td>American College of Rheumatology</td>
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<td>JNC VII</td>
<td>Seventh Report of the Joint National Committee</td>
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<td>HTN</td>
<td>Hypertension</td>
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<td>WHR</td>
<td>Waist hip ratio</td>
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<td>OR</td>
<td>Odds ratio</td>
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<td>IgM</td>
<td>Immunoglobulin M</td>
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<tr>
<td>MOPC</td>
<td>Medical outpatient clinic</td>
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<tr>
<td>TNF</td>
<td>Tumor necrosis factor</td>
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<tr>
<td>CV</td>
<td>Cardiovascular</td>
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<tr>
<td>LDL-C</td>
<td>Low density lipoprotein cholesterol</td>
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<tr>
<td>HDL-C</td>
<td>High density lipoprotein cholesterol</td>
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<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>ACS</td>
<td>Acute coronary syndrome</td>
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<tr>
<td>TIA</td>
<td>Transient ischemic attack</td>
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<td>CABG</td>
<td>Coronary artery by pass graft</td>
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<td>NCEP</td>
<td>National cholesterol education programme</td>
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ABSTRACT

Introduction and background

Rheumatoid arthritis is associated with excess cardiovascular morbidity and mortality predominantly due to accelerated coronary artery and cerebrovascular atherosclerosis.

Objective:

To identify traditional cardiovascular risk factors in patients with rheumatoid arthritis at Kenyatta National Hospital and compare with healthy controls

Study design/site:

This was a descriptive comparative cross sectional survey done at KNH medical outpatient clinic. The study population consisted of patients with rheumatoid arthritis and the controls were individuals without RA age and sex matched staff of KNH. All those who consented were enrolled and a clinical evaluation was done. Consecutive sampling was done on those who fulfilled ACR criteria for patients with RA and also for the controls who consented to participate in the trial.

Methodology

The patients/controls who met inclusion criteria and signed an informed consent, filled a questionnaire with the help of an assistant and had their weight, height, Blood pressure, waist circumference, hip circumference measured. Blood was also taken for fasting blood sugar and lipid profile analysis. They were given back their results and accorded treatment according to the outcome of their results.

Results

One hundred patients with RA were screened out of which 80 were enrolled. In the control group one hundred and five were screened, twenty five were excluded and 80 were enrolled. The prevalence of hypertension among RA patients was 41.3 % (24.4-58.1) Vs 22.5% (3.2-41.8) in the control group and this was statistically significant (P = 0.017). Diabetes in RA patients was 6.3% Vs 5% (p =1) in the controls, prevalence of dyslipidemia in RA patients was 71.3 % (59.6-83) Vs 73.8 % (62.6-85) in the control group (p =0.723). The prevalence of smoking in RA patients was 5% Vs 2.5% (p=0.681) in the control group, while the prevalence of obesity was 22.5% in the patients with RA Vs 32.5% in the control group (p=0.157). Study participants with abnormal WHR were 33.8% in those with RA Vs 33.8% in the control group. Family history of sudden death in
patients with RA was 5% Vs 10% in the controls, no family history of stroke or heart attack was reported in the patients with RA. Ten percent of the controls had a family history of sudden death. Family history stroke was 1.3% in the controls and no history of heart attack was reported in the control group. Eighty percent of patients with RA were on at least one DMARD, 57.5% were on steroids and 37.5% were on NSAIDS.

**Conclusion**

There is a high prevalence of hypertension in patients with RA; hypertension was also associated with the use of DMARDs and steroids and this was statistically significant. There was no significant difference between patients and controls in terms of other risk factors such as diabetes mellitus, dyslipidemia, smoking, BMI, WHR, and family history of cardiovascular events.

**Recommendations**

Clinicians should keenly look out for hypertension in patients with RA for early identification and manage it appropriately.
CHAPTER ONE
1.0 INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

Rheumatoid arthritis is a chronic systemic autoimmune inflammatory disorder. It is characterized by deforming symmetrical polyarthritis of varying extent and severity, associated with synovitis of joint and tendon sheaths, articular cartilage loss, erosion of juxta-articular bone and, in most patients, the presence of IgM rheumatoid factor in blood. In some patients systemic and extra-articular features may be observed during the course of the disease and, rarely prior to onset of joint disease.

Criteria and methods for diagnosis for rheumatoid arthritis have varied in different epidemiological studies; however in recent years there has been a tendency towards a more widespread use of American college of Rheumatology (ACR) criteria thus introducing a measure of standardization. The American college of rheumatology has diagnostic criteria in which four of seven criteria are required to classify a patient as having RA (Appendix 5).

Hypertension is one of the most common worldwide diseases afflicting humans. Because of the associated morbidity and mortality and the cost to society, hypertension is an important public health challenge. Hypertension is the most important modifiable risk factor for coronary heart disease, the leading cause of death in North America, stroke, congestive heart failure, end-stage renal disease, and peripheral vascular disease. Recent data from the Framingham Heart Study suggest that individuals who are normotensive at 55 years of age have a 90% lifetime risk for developing hypertension.

A study done by Han and colleagues, showed that individuals with rheumatoid arthritis are 30% to 60% more likely to suffer a cardiovascular event compared to the general population, especially myocardial infarction. One study done by Turesson et al found a higher prevalence of stroke in patients with rheumatoid arthritis than in controls. We do not have local data in Kenya to support these findings. A few studies have been done
locally on rheumatoid arthritis and so far there has been no study looking at the cardiovascular risk factors in patients with rheumatoid arthritis.

In the quest RA study, Univariate analysis done showed that all traditional cardiovascular risk factors except obesity and physical inactivity were associated with cardiovascular morbidity, and in the multivariate models, hypertension, hyperlipidemia, diabetes and ever smoking remained independent risk factors. This supported the role of traditional cardiovascular risk factors concerning cardiovascular morbidity in patients with rheumatoid arthritis. We do not know whether these findings are applicable in our setup and this study would answer some of these questions.

The use of methotrexate has been associated with a significant lower risk for cardiovascular events in rheumatoid arthritis patients compared to patients who had never used DMARDS. We would like to determine the proportion of patients using methotrexate and other DMARDs in our study population and look for any associations with cardiovascular disease.

It is important to identify cardiovascular risk factors in patients with rheumatoid arthritis so as to identify individuals at risk. This may go along way in decreasing the resultant morbidity and mortality in this patient population. With the data from this study we will able to have a baseline data to guide us in developing protocols and education of health care professionals. The study will act as an entry for other studies to be done on emerging themes in the area of rheumatology.

1.2 Literature review
Rheumatoid arthritis (RA) is a chronic systemic disease with articular and extra-articular manifestations. It is a common disorder, affecting people of all ethnic groups worldwide. The prevalence of RA is approximately 0.8% of the entire population globally (range 0.3 to 1.2); women are affected approximately three times more often than men. The prevalence increases with age and, sex differences diminish in older age group. Rheumatoid arthritis is seen globally and affects all races, however the incidence and
severity seem to be less in rural sub Saharan Africa and Caribbean blacks 8,9 the onset of disease is most frequent during the fourth and fifth decade's of life, with 80% of all patients developing the disease between the ages of 35 and 50 years 10.

The prevalence of RA in the general population in Europe and US is between 0.8 and 1.1 percent from cross sectional studies 1. A striking high prevalence rate of 4 to 5 percent has been noted among some Native American populations, for example the Pima and Chippewa Indians 1. Lower prevalence of 0.2 to 0.3 percent has been reported in China and Japan 1. The prevalence of RA amongst black population is low in rural South Africa (Approx 0.2%), whereas prevalence rates of almost 1 percent have been observed among black populations in urban black South Africans and in the US 11. There has been a changing pattern in prevalence and severity of RA in Africa. Earlier studies suggested that RA was a rarity in sub-Saharan Africa11. A report from Nigeria by greenwood in 1969 12 has suggested that it was not an important cause of admission to hospital in this country.

In a study carried out in Kenya by Houba et al in 1979 13 sera from 48 Kenyan Africans with RA, 43 patients with other diseases and 98 blood donors were tested for presence of rheumatoid factor by various latex fixation tests. In patients with RA the frequency of Rheumatoid factor was comparable to that reported in series from Europe and USA. In the control patients and blood donors a high frequency of positive tests for rheumatoid factor was found. A similar result was found from population studies in other African countries results 13.

Owino and colleagues was able to see 60 patients within a period of six months at KNH MOPC (MMED dissertation 2007) as compared to Bagg et al 14 who in 1979 was able to see 76 patients over a period of 18 months. This rise in number of cases could have been to a reflection of an improved referral system or increased urbanization in Kenya, as studies in South Africa and USA have shown increased prevalence of rheumatoid arthritis in urban populations as compared to rural population. On the other hand it could be due
to increase of the population of Nairobi. These can only be ascertained by conducting well designed trials.

1.3 Etiology of Rheumatoid arthritis

The causes of rheumatoid arthritis are unknown, but there is a genetic predisposition in that various HLA-DR4 genotypes are associated with an increased incidence and severity of disease in different populations. The HLA associations support the hypothesis that particular HLA DR molecules present antigens to T cell receptors and activate pathogenic reactions. On the other hand some HLA DR subtypes have negative correlation with RA therefore different signals to T-cells appear to constitute regulatory pathways.

Concordance rates of monozygotic twins and dizygotic twins from studies in western populations strongly favor multigenic influence and argue for an environmental trigger. Environmental factors such as cigarette smoking have been associated with increased risk of rheumatoid arthritis in two prospective population studies and one twin study. Other environmental factors implicated for example viruses have proven speculative. Host factors such as sex hormones or prolactin are implicated in susceptibility or protection in RA for example RA is commoner in females especially premenopausal than males. Contraceptive pill confers protection by delaying onset of RA and rheumatoid arthritis is suppressed during pregnancy.

1.4 Rheumatoid arthritis and cardiovascular disease

Patients with Rheumatoid arthritis (RA) experience an increased burden of cardiovascular disease (CVD) and reduced life span compared with the general population. Cardiovascular (CV) events occur approximately a decade earlier in RA than in the general population suggesting that RA, similarly to diabetes mellitus, is an independent risk factor for premature ischemic heart disease. Epidemiological studies have shown that Rheumatoid arthritis is associated with increased mortality rates and this increased mortality is attributable to cardiovascular disease, primarily coronary heart disease.

The increased mortality is predominantly due to accelerated coronary artery and cerebrovascular atherosclerosis a phenomenon that occurs in early and established
rheumatoid arthritis. The accelerated atherosclerosis seen in RA is due to indirect effect of inflammation centered on synovium, acting at a distance on systemic vascular endothelium. Although inflammation in RA centers on synovial tissue, inflammation mediators spill into systemic circulation where they can easily interact with endothelial cells.

Interleukin 1 (IL-1) and tumor necrosis factor alpha (TNF alpha), 2 of the central cytokines in RA are found in high concentrations in blood of RA patients. These mediators of inflammation have profound effects on endothelial cells, upregulating them to express adhesion molecules, increasing their permeability, and facilitating migration of inflammatory cells into vessel walls. C-reactive protein (CRP), the level of which rises in periods of RA disease activity, may also play a direct role in atherothrombosis. CRP stimulates macrophages to produce tissue factor, an important procoagulant that may be found in atherosclerotic plaques.

1.4.1 Hypertension

Hypertension (HT) is one of the most important modifiable classical CVD risk factors in the general population and is very common in patients with rheumatoid arthritis. In the INTERHEART Study, hypertension accounted for 18% of the population attributable risk of a first myocardial infarction (MI). Hypertension increases the risk of cardiovascular disease both in general population and in rheumatoid arthritis patients. Rheumatoid arthritis (RA) is associated with increased cardiovascular mortality due to increased prevalence of co-morbidities such as myocardial infarction (MI), stroke and heart failure (HF). The adjusted relative risk of myocardial infarction in women with RA compared to those without RA is estimated to be around 2.0. While acute coronary syndromes may present atypically and recur more frequently in patients with Rheumatoid arthritis, increased clinical suspicion may aid early identification and appropriate management of risk factors in these patients.

Hypertension is quantitatively the most important modifiable risk factor for cardiovascular disease (CVD), being more common than cigarette smoking, dyslipidemia
or diabetes. It remains unclear whether hypertension is commoner in people with RA than in those without RA. Ageing and obesity are known predictors of hypertension in the general population; smoking and low-grade inflammation may also contribute to the development of hypertension. In RA, the chronic inflammatory burden may lead to increased arterial stiffness, one of the physical causes of raised systolic blood pressure (BP), providing a potential link between inflammation and hypertension in this disease.

The QUEST RA study (which was a multinational cross sectional cohort of non selected consecutive out patients with RA) showed that all traditional cardiovascular risk factors except obesity and physical inactivity were significantly associated with cardiovascular morbidity. In the multivariate models, hypertension, hyperlipidemia, diabetes and ever smoking remained independent risk factors. These supported the influence of traditional cardiovascular risk factors and RA specific risk factors in the development of cardiovascular events especial myocardial infarction. A study done by Han and colleagues study found a higher prevalence of stroke in patients with rheumatoid arthritis than in controls.

1.4.2 Dyslipidaemia

Epidemiological studies have shown a strong relation between serum total cholesterol and cardiovascular risk and that Changes in cholesterol levels due interventions were associated with changes in CVD incidence rate. Elevated LDL cholesterol are associated with increased risk of coronary heart disease and therapeutic strategies that lead to a statistically significant reduction in LDL cholesterol lower CHD event rates. Oxidative modification of LDL may also be important and it is of interest that oxidised LDL has been noted in RA synovial biopsy specimens. Products of LDL oxidation may be recognized by the scavenger receptor leading to increased uptake of the modified lipoprotein particle by macrophages; they may be directly cytotoxic to endothelial cells, chemotactic for inflammatory cells, and cause functional changes in smooth muscle. The inflammatory environment and disturbed antioxidant mechanisms in RA may promote LDL oxidation, thereby facilitating atherogenesis at lower ambient lipid
concentrations and placing RA patients at higher cardiovascular risk. Some studies have shown that total, LDL and HDL cholesterol and triglycerides are reduced in active RA compared with inactive disease, non-inflammatory arthritis or normal controls, with inverse correlation between lipid values and the acute phase response.

1.4.3 Smoking

Substantial evidence suggest that individuals who smoke are more likely to develop rheumatoid arthritis and that patients with RA who smoke are more likely to have more severe disease. Thus it is possible that smoking a potent risk factor for atherosclerosis interacts with rheumatoid arthritis to accelerate atherosclerosis to a greater degree in patients with this disease. Substantial evidence also indicates that inflammation can accelerate atherosclerosis and markers and drivers of inflammation such as the level of CRP are elevated in patients with coronary artery disease. The rise in CRP serves as predictor for cardiovascular disease and therefore, premature atherosclerosis could represent a consequence of chronic inflammation as occurs with RA.

1.4.4 Diabetes

Diabetes is associated with a 2- to 3-fold increase in the likelihood of developing cardiovascular disease, this increase being higher in women than in men. Glucose intolerance is also associated with a 1.5-fold increase in the risk of developing cardiovascular disease. Moreover, diabetes is also associated with a higher probability of presenting with hyper triglyceridemia, low HDL-C, high blood pressure, and obesity, which usually precede the onset of diabetes. A study done in South Africa showed that insulin resistance and diabetes mellitus is common among patient with RA than in the controls.

1.4.5 Physical Inactivity
A number of epidemiological studies have confirmed an association between physical inactivity and coronary heart disease (CHD). The relative risk of death from CHD forsedentary compared with active individuals is 1.9 (95% confidence interval 1.6-2.2).

Physical inactivity is common in general population and a frequent consequence of arthritis. A trial in done in South Africa demonstrated that patients with RA exercised less frequently than the healthy controls while another trial found patients with RA exercised more frequently than those with osteoarthritis. In the general population, the frequency of weekly physical activity of three or more times is associated with reduced cardiovascular morbidity.

1.4.6 Obesity

Obesity is a chronic metabolic disorder associated with numerous co-morbidities such as coronary heart disease, cardiovascular disease, type 2 diabetes, hypertension, certain cancers and sleep apnea. Obesity is also an independent risk factor for all-cause mortality. Obesity particularly central obesity is associated with an increased risk of cardiovascular risk. In addition to alterations in metabolic profile, various adaptations in cardiac structure and function occur as excess adipose tissue accumulates.

Similar to data observed with LDL-C and supporting the idea that the progression of atherosclerosis should be viewed as a continuous process beginning early in life, a recent study reported that higher BMI during childhood is associated with an increased risk of CHD in adulthood. This association seems to be stronger in boys than in girls and increases with the age of the child in both sexes.

In the INTERHEART study, a marker of abdominal obesity with either the waist – hip ratio or the waist circumference, was a better predictor of myocardial infarction in all ethnic groups, than the Body Mass Index (BMI). Due to the shape of the African figure, particularly in women, it has been suggested that the Waist circumference alone rather than the Waist Hip Ratio is a better indicator of abdominal obesity in this population. A study done by dessein and colleagues on patients with RA and healthy controls found
that; the body mass indices were similar in both groups, but patients with RA had higher waist circumference, blood pressure and triglyceride levels 

1.4.7 Hyper homocysteinemia
An elevated serum concentration of homocysteine is a known risk factor for atherosclerosis and is associated with an increased risk of myocardial infarction and death. The risk appears to be greater in patients with diabetes. High levels of homocysteine are commonly found in patients with rheumatoid arthritis (RA), thus accounting, at least in part, for the high rate of mortality for cardiovascular events in these subjects. The mechanisms responsible for hyper homocysteinaemia in RA are not clear. However, drugs such as methothrexate and sulfasalazine affect homocysteine metabolism, interfering with vitamin metabolism and absorption. Furthermore, an increased use or accelerated catabolism of vitamin B6 has been shown in chronic inflammatory diseases, particularly RA.

1.4.8 Dietary factors
In a large number of observational studies and their meta-analyses, individuals who consume fewer calories, more fruits and vegetables, and less saturated fats tend to have lower risks of CAD. The increased availability of energy dense foods poor in dietary fiber and several micronutrients, plus a shift from plant to animal protein and shifts towards refined carbohydrates are important aspects of the nutritional transition observed in sub-Saharan Africa. The result has been an increasing prevalence of abnormal lipid profiles and impaired glucose tolerance.

1.4.9 Family history
An analysis from the Framingham Offspring Study evaluated the CAD risk in offspring of the original Framingham Heart Study cohort. After adjustment for other risk factors, parental history was significant for CAD risk. A study done in Minnesota in the US found no difference in the family history of CAD in patients with RA and normal population controls.
1.4.10 Drugs used in treatment of rheumatoid arthritis

Drugs commonly administered to RA patients may cause major or minor increments in BP levels. This includes: Non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase II inhibitors (Coxibs)\(^{38}\), oral steroids \(^{39}\) and some disease-modifying anti-rheumatic drugs (DMARDs), such as leflunomide \(^{60}\) and cyclosporine\(^{61}\).

1.4.11 Glucocorticoids

Low dose oral glucocorticoids (<10mg of prednisone daily, or equivalent) and local injections of glucocorticoids are highly effective in relieving symptoms in patients with active RA.\(^{62}\).

A study by Panoulas \textit{et al} \(^{63}\) showed that RA patients exposed to medium oral daily prednisone doses ≥7.5mg for long periods (>6 months) are significantly more likely to be hypertensive than RA patients who have no or limited exposure, or receive low dose (<7.5mg) oral daily prednisone. This appeared to be independent of other risk factors for hypertension or of channeling bias due to disease severity, even though the latter could not be excluded given the cross sectional nature of the study. Several studies\(^{64}\) have shown that increased cortisol secretion and action even within the normal range is associated with hypertension.

1.4.12 Disease modifying anti rheumatic drugs (DMARDs)

A Meta analysis of blinded clinical trials has suggested that the efficacy of methothrexate (MTX), sulfasalazine (SSZ), intramuscular gold, and penicilamine is similar\(^{65}\). Use of hydroxychloroquine in patients with RA has demonstrated reduction of 15-20% in serum triglyceride, cholesterol, and LDL concentrations and a reversal of the lipid-raising effects of corticosteroids\(^{66}\). Use of DMARDs especially MTX and SSZ have been associated with lower risk for CVD in patients with RA.\(^{5}\)

1.4.13 Biologic DMARDS

The biologic products that inhibit the actions of TNF-alpha include infliximab, etanacept, adalimumab and rituximab. Anakinra that inhibits action of interleukin 1 are now being
used in the management of RA. Randomized controlled trials have demonstrated that triple DMARD combination of MTX, SSZ, and hydrochloroquin (HCQ) has substantially increased efficacy compared to MTX alone or to HCQ plus SSZ without increased toxicity.  

2.0 JUSTIFICATION OF STUDY
Rheumatoid arthritis is associated with a lot of morbidity and mortality due to cardiovascular disease. This is predominantly due to accelerated coronary artery and cerebrovascular atherosclerosis. It has been shown that cardiovascular events occur, a decade earlier in patients with RA than in the general population and these patients have also traditional cardiovascular risk factors that may predispose to developing cardiovascular disease earlier than individuals who don't have RA.

We do not have local data documenting burden of traditional cardiovascular risk factors in our population with RA. The results from baseline study will address these issues and will guide in formulating strategies for intervention of these risk factors in our local population with RA. This will be done by providing appropriate treatment to those who have cardiovascular risk factors.

2.1 RESEARCH QUESTION.
What is the prevalence of traditional cardiovascular risk factors in patients with rheumatoid arthritis attending Medical outpatient Clinic at Kenyatta National Hospital.

2.3.0 OBJECTIVES
2.3.1 General Objectives
To identify cardiovascular risk factors in patients with rheumatoid arthritis at Kenyatta National Hospital

2.3.2 Specific primary objectives
1 To determine prevalence of hypertension in patients with rheumatoid arthritis and controls
2. To determine the prevalence of diabetes in patients with RA and controls

3. To determine the prevalence of dyslipidemia in patients with RA and controls

4. To determine prevalence of smoking in patients with rheumatoid arthritis and controls

5. To determine anthropometric measurements (BMI, WHR) in patients with RA and controls

6. To determine family history of cardiovascular events such as sudden death, MI or stroke and controls

7. To compare the cardiovascular risk factors in patients with rheumatoid arthritis with the controls

2.3.3 Specific secondary objectives

1. To document cardiovascular events (stroke, MI, HF) in patients with RA

2. To document the use of DMARDs, steroids, NSAIDS, biologic DMARDs, antihypertensive medication in hypertensive patients with RA, anti-diabetics, statins, and aspirin in patients with RA
CHAPTER 3
MATERIALS AND METHODS
3.0 METHODOLOGY
3.1 Study design
This was a descriptive comparative cross sectional survey

3.2 Study site
The study was done at the Medical out Patient Clinics (MOPC) at Kenyatta National Hospital

3.3 Study population
These were patients above eighteen years; clinically diagnosed to have rheumatoid arthritis according to ACR criteria (Appendix 5) attending MOPC at Kenyatta National Hospital. The controls were individuals without RA and these included healthy employees from Kenyatta National Hospital, it included nurses, clinicians and support staff working and students doing internship at various departments at the hospital.

3.4.1 Inclusion criteria for cases
- Above 18 years
- Confirmed to have rheumatoid arthritis as per ACR criteria
- were willing to participate and signed an informed consent

For the controls
- Healthy individuals above 18 years age and sex matched.
- Confirmed not to have Rheumatoid arthritis as per ACR criteria

3.4.2 Exclusion criteria
- Not willing to participate in the study
3.5 Sample size determination

Based on the current data available with a prevalence of 30% (6) for hypertension in these population at 95% confidence interval and a 5% margin of error the minimum sample size needed was. Hypertension was used so as to get the minimum sample size required.

\[
n = \frac{[z^2 \sqrt{2p(1-p)} + z_{1-\beta} \sqrt{(p_1(1-p_1) + p_2(1-p_2))}}}{(p_1-p_2)^2}
\]

\(n=\) sample size
\(z=1.96(\)the corresponding value to power of 95\%\)
\(p=\frac{P_1+P_2}{2}\)
\(P_1 = 30\%\)
\(P_2 = 10\%\)
\(Z_{1-\beta} = \) power
\(80\% \ Z_{1-\beta} = 0.842\)

\[
n = \frac{[1.96 \sqrt{2 \times 0.2 \times 0.8} \times 0.842 \sqrt{(0.3 \times 0.7)} + (0.1\times 0.9)]^2}{(0.2)^2} = 80
\]

An estimated minimum sample of 80 patients with rheumatoid arthritis and 80 controls were recruited. Total = 160

3.6 SCREENING AND RECRUITMENT

3.6.1 Clinical procedures in patients with RA

The principal investigator/assistant went to the MOPC and identified files of those patients suspected to have RA as per their complaints, clinical signs and laboratory results documented in their files. Patients found to have rheumatoid arthritis as per the American college of rheumatology criteria \(^6\) were invited to participate in the study and all those who met inclusion criteria were informed about study. See the attached appendix for ACR criteria for RA. Written informed consent was then sought from the patient /
guardian for patients who were unable to give consent. Only the patients who gave consent were recruited into the study. Baseline demographic and socio-economic data was collected from these clients using standardized questionnaires. The principal investigator who was a senior house officer administered the questionnaire to the patients/controls by asking questions according to the questionnaire format. The questionnaire captured data on sex, marital status, level of education, employment and duration of illness/treatment for the patients with RA.

A detailed review of their medical history and hospital records, a family history of sudden death, myocardial infarction or stroke and also a history of smoking by the patient with RA was taken. A physical examination, assessments of height in meters, weight in kilograms waist/ Hip circumference in centimeters and blood pressure measurements in mmHg was obtained. All the clinical findings, measurements and the medications with their exact indications were recorded. We also documented any evidence of heart failure, myocardial infarction or stroke from the clinical examination findings with the help of investigations from their hospital records. The study assistant helped in tracing those who have been booked for a fasting lipid profile and a transport allowance was given to those who were rebooked for follow up.

Controls
Age and sex matched staff from Kenyatta National Hospital and students doing internship at various departments at the hospital. The principal investigator went to the various work places and placed posters detailing on the study objectives, recruitment and enrollment procedures for the staff working at KNH. Small meetings were organized at work place where the principal investigator would talk to a group of nurses, clinical officers and support staff informing them on the objective of the study. Those who volunteered to participate were screened and those found not to have rheumatoid arthritis were enrolled into the study. Age was matched to the nearest 5 years. After consenting, further clinical exam, blood pressure and anthropometric measurements weight, height, waist, and hip circumference were taken. Any co morbidities and drug therapy was also recorded.
Blood pressure (BP) measurement

A mercury sphygmomanometer was used in measuring the blood pressure. The recorded blood pressure was the mean of two measurements taken at 5 min intervals on the right arm with the patient in a seated position after at least 5 min rest, using an appropriately sized cuff. Cuff bladder encircled 80 percent or more of the patients arm circumference and the ideal width was at least 40 percent of the arms circumference. We utilized korotkoff's phase I and IV as systolic and diastolic pressure respectively.

Measurement of Waist Hip Circumference

The waist circumference was taken as the narrowest circumference between the lowest rib and the top of the pelvis, measured in the horizontal plane. The hip circumference was taken as the maximum circumference measured at the buttocks in the horizontal plane over the greater trochanter. A tape measured calibrated in centimeters/meters was used to take the above measurements. The patient/control was asked to remove shoes and any heavy clothing such as jackets and items in the pocket and were asked to stand on the weighing scale after which there measurements were read and recorded. The patient/control was asked to stand straight along the wall where a height scale meter was placed; after removing shoes and caps on their head. They had their height measured and recorded. The patient/control weight in kilograms and height in meters were taken for the calculation of BMI.

3.6.2 Laboratory procedures

The subjects/controls had their blood drawn from ante-cubital fossa for fasting blood sugar and lipid profile. The clients who had fasted are the ones who had taken their last meal (super) more than 8 hours prior to their scheduled appointment that morning. For clients who had fasted that morning, a fasting lipid profile was done. 2 ml of blood was drawn and put into a plain vacutainer bottle. The samples were assayed with commercially available kits, manufactured by Human diagnostics world wide (Germany), at the department of internal medicine laboratory. If the volunteers had taken their breakfast they were asked to come the following day for a fasting lipid profile to be done.
A blood sugar was done using the glucose meter with test strips and using Accu-Check glucometer manufactured by Roche diagnostics, Indianapolis, (US).
PATIENT FLOW CHART

PATIENTS SUSPECTED TO HAVE RA

CONSENT

YES

NO

EXCLUDE FROM THE

EXCLUDE FROM THE STUDY

FULLFILLING ACR CRITERIA

YES

NO

CONTROLS

CONSENT

YES

NO

Exclude

HISTORY/CLINICAL EXAM BP/BMI/ONNAIRE

FASTED

YES

LIPID/PROFILE/FASTING RBS

NO

NEXT APPOINTMENT

FASTING LIPID PROFILE/FASTING RBS
3.7 Defining of Study Variables

Rheumatoid arthritis (Cases)

Were patients with rheumatoid arthritis confirmed as per ACR criteria (Appendix 5)

Hypertensive Status

Patients were defined as hypertensive by either:

The current use of hypertensive medication, WHO criteria for hypertension: Systolic BP >140 mmHg and / or Diastolic BP of > 90mmHg

Controls

Were healthy individuals not having rheumatoid arthritis. They were employees from Kenyatta National Hospital; they included the nursing staff, clinical officers, doctors and support staff from Kenyatta National Hospital.

Cardiovascular disease

Patients were classified as having CVD if they had a positive history of any of the following: Heart failure, Myocardial infarction, Stroke or Transient ischemic attack (TIA), Peripheral vascular disease (PVD), prior angioplasty, Coronary Artery by pass grafting (CABG).

Heart failure was defined by a history or documentation of heart failure by the clinicians seeing the patient.

Waist Circumference

Central Obesity was defined according to the NCEP / ATP III by a waist circumference of >/= 102cm in males and >/= 88 cm in females.

Waist Hip Circumference Ratio

Defined by WHO criteria as abnormal if the ratio >0.90 in males and >0.85 in females. Any value high than this in males and females was defined as abnormal in this study.
Use of Alcohol
Patients were classified as:
Never
Current (quantity and duration defined)
Former (Period of abstinence defined)

Smoking
The patients were classified as:
Never smoked
Current smoker (last smoked within the last year) / pack years defined
Former smoker (last smoked > 1 year ago) and period of abstinence defined.

Dyslipidaemia
Adult Treatment Panel III guidelines for the management of serum lipids for high risk patients including those with a coronary artery disease equivalent, the lipid profile was classified as shown in appendix 7. Dyslipidemia was defined as anyone with abnormality of any subtypes of the lipid profile.

Diabetes
Patients will be defined as being diabetic when fasting glucose levels is >7mmol/ and or on oral hypoglycemic medication or insulin was used, or a patient with symptoms of; diabetes and a random blood glucose concentration of more than11.1 mmol/L.

Obesity and BM I

BMI calculation and classification
It is defined as the weight in kilograms divided by the square of the height in meters (kg/m$^2$). See attached appendix 4 for international classification by WHO.

\[
BM I = \frac{Weight (kg)}{Height^2 (M^2)}
\]

Obesity was defined for those patients /controls with a BMI over 30
3.8 Data management and analysis

All data was collected from pre printed forms and entered into software data management program (MS ACCESS). It was cleaned and verified to ensure that quality was maintained. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 15.0 (SPSS Inc, Chicago, IL, USA). Primary categorical variables that were examined included; hypertension, diabetes, dyslipidemia, obesity and smoking. Continuous demographic variables included; age, height. Descriptive statistics on continuous variables included the mean, standard deviation, median, minimum and maximum. Descriptive statistics of categorical variables used frequencies. All was done with the corresponding 95% confidence intervals.

Comparison of categorical variables was examined using Chi-square test or Fischer’s exact test where applicable. Correlations between variables were tested using spearman’s correlation coefficient in case it was a continuous variable; for categorical variable association was done using Pearson’s Chi square. Prevalence was estimated from proportions calculated within 95% confidence interval. Statistical significance was defined by two tailed p value of less than or equal to 0.05. Data is presented in tables, graphs and pie charts.

3.9 Ethical considerations

This study had minimal risk to subjects. Patients/controls consented for their participation by signing a consent form. They received a free blood pressure, lipid profile, fasting blood sugar which was placed in their clinic file and in cases where there were abnormal results the attending clinician would be informed about it so as to give the appropriate treatment. Institutional review board approval was sort and obtained from the Department of Clinical Medicine & therapeutics, University of Nairobi and from Kenyatta National Hospital Ethical Review board before data collection. Patients/control with high blood pressure benefited from free diagnosis and treatment given to them appropriately.

All patients had the opportunity to have the forms explained to them and to asked questions from the investigator prior to study enrolment. They had the right to withdraw consent at any time. Patients were assigned a study number at enrollment. This number
was used to identify patients for all matters related to data analysis. The forms linking patient names and demographic information to particular ID numbers was kept locked in a file at the office of the Investigator. Access to this office and the data was restricted to the investigator.
CHAPTER 4
4.1 RESULTS

One hundred patients with or suspected to have RA were screened for recruitment out of which 20 were excluded from the study. Among the control group one hundred and five healthy individuals were screened out of which twenty five were excluded from the study for several reasons like refusing consent or were lost to follow up (see recruitment flow chart below).

Screening and recruitment was done consecutively and this was done at the various MOPCs at Kenyatta National Hospital. An average of 5 cases and 5 controls were enrolled per week and recruitment period was from November 2008 and ended in February 2009. A total number of 160 cases and controls were enrolled, 22 (13.75%) were males and 138 (86.25%) were female. (Table 1)

Recruitment Flow CHART

**Cases**

- 100
- 96
- 88 Fulfilled ACR criteria
- 80 Enrolled
- 4 Refused consent
- 8 not fulfill ACR criteria
- 8 Lost to follow up

**Controls**

- 105
- 90
- 80 Enrolled
- 15 refused consent
- 10 lost to follow up
The mean age for patients with RA was 44.7 years, the median age 48 years and [range was 18 to 75 years]. For the healthy individuals without RA, the mean age was 44.6 years, the median was 43 years and [range was 22 to 75 years]. (Table 1) There were two peaks of disease in the patients with RA with the peaks at age ranges 20-29 and 50-59 years. (Figure1)

Table 1: Demographic characteristics of patients with Rheumatoid Arthritis and healthy controls

<table>
<thead>
<tr>
<th>Variables/categories</th>
<th>Case n (%)</th>
<th>Control n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11(13.8)</td>
<td>11(13.8)</td>
<td>22(13.8)</td>
</tr>
<tr>
<td>Female</td>
<td>69(86.2)</td>
<td>69(86.2)</td>
<td>138(86.2)</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>56(70)</td>
<td>47(58.8)</td>
<td>103(64.4)</td>
</tr>
<tr>
<td>Single</td>
<td>19(23.8)</td>
<td>24(30)</td>
<td>43(26.9)</td>
</tr>
<tr>
<td>Widowed</td>
<td>3(3.8)</td>
<td>8(10)</td>
<td>11(6.9)</td>
</tr>
<tr>
<td>Divorced</td>
<td>2(2.5)</td>
<td>1(1.3)</td>
<td>3(1.9)</td>
</tr>
<tr>
<td><strong>Level of education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4(5)</td>
<td>2(2.5)</td>
<td>6(3.8)</td>
</tr>
<tr>
<td>Primary</td>
<td>28(35)</td>
<td>10(12.5)</td>
<td>38(23.8)</td>
</tr>
<tr>
<td>Secondary</td>
<td>15(18.7)</td>
<td>9(11.3)</td>
<td>24(15)</td>
</tr>
<tr>
<td>College</td>
<td>20(25)</td>
<td>47(58.7)</td>
<td>67(41.9)</td>
</tr>
<tr>
<td>Tertiary</td>
<td>13(16.3)</td>
<td>12(15)</td>
<td>25(15.6)</td>
</tr>
<tr>
<td><strong>Employment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>24(30)</td>
<td>20(25)</td>
<td>44(27.5)</td>
</tr>
<tr>
<td>Employed</td>
<td>29(36.3)</td>
<td>48(60)</td>
<td>77(48.1)</td>
</tr>
<tr>
<td>Self employed</td>
<td>19(23.7)</td>
<td>8(10)</td>
<td>27(16.9)</td>
</tr>
<tr>
<td>Retired</td>
<td>8(10)</td>
<td>4(5)</td>
<td>12(7.5)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>44.7±15.3(18-75)</td>
<td>45.0±13(22-75)</td>
<td>44.8 ± 14.2 (18 - 75)</td>
</tr>
<tr>
<td>Median</td>
<td>48</td>
<td>43</td>
<td>45</td>
</tr>
</tbody>
</table>
4.2 Cardiovascular risk factors

Figure 1: Age distribution of patients with Rheumatoid arthritis.

Thirty three patients (41.3% (24.5-58.1) with rheumatoid arthritis had hypertension compared to eighteen (22.5 % (3.2-41.8) healthy controls. This difference was highly statistically significant, (O.R 2.42 (95 C I 1.22-4.81) P = 0.017) Table 2. Five (6.3%) patients with rheumatoid arthritis had diabetes while 4(5%) controls had diabetes mellitus. When the two groups were compared there was no statistically significance. (O.R 1.28 (95 C I 0.33-4.90) P =1.0). Fifty seven patients with RA (71.3% (59.6-83) had dyslipidemia, likewise almost a similar number of 59 (73.8% (62.6-85) of the healthy controls had dyslipidemia.(O.R 0.97 (95 C I 0.44-1.77) P =0.723). Table 2
Four (5%) patients with rheumatoid arthritis smoked and two (2.5%) healthy controls smoked cigarette. The cases were twice more at risk of smoking than the controls however, no statistical significance was observed in this study. O.R 2.05 (95 C I 0.09-2.74) P =0.687. Eighteen (22.5% (3.2-41.8)) patients with rheumatoid arthritis were obese while 26 (32.5 % (14.5-50.5) in the controls were obese. O.R 0.603 (95 C I 0.299-1.218) P =0.157 Table 2.

Twenty seven (33.7 % (16-51.6) of patients with rheumatoid arthritis had a high waist hip ratio, a similar number was observed in the control group and when they were compared there was no statistical significance. O.R 1 (95 C I 0.519-1.926) P =1.0. There was no family history of myocardial infarction among the patients with rheumatoid arthritis and the healthy controls, one person from the controls reported a family history of stroke. Four patients with RA reported a family history of sudden death while eight individuals in the healthy control group reported a family history of sudden death; however, this was not statistically significant. OR 0.47 95%CI (0.137-1.641) P = 0.369. Only one patient with RA reported past history of Heart failure; none of the patients with RA or healthy controls reported a previous history of myocardial infarction or stroke. Table 2
### 4.3: Analysis

#### Table 2: Bivariate analysis on correlates of cardiovascular risk factors in patients with Rheumatoid arthritis and healthy controls

<table>
<thead>
<tr>
<th>Factors</th>
<th>Case</th>
<th>Control</th>
<th>P. value</th>
<th>O.R</th>
<th>95% C.I O.R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>33(41.3%)</td>
<td>18(22.5%)</td>
<td>0.017</td>
<td>2.42</td>
<td>1.22-4.81</td>
</tr>
<tr>
<td>No hypertension</td>
<td>47(58.7%)</td>
<td>62(77.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>5(6.3%)</td>
<td>4(5%)</td>
<td></td>
<td>1.27</td>
<td>0.33-4.90</td>
</tr>
<tr>
<td>No diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>4(5%)</td>
<td>2(2.5%)</td>
<td>0.681</td>
<td>2.05</td>
<td>0.09-2.74</td>
</tr>
<tr>
<td>No smoking</td>
<td>76(95%)</td>
<td>78(97.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal WHR</td>
<td>27(33.8%)</td>
<td>27(33.8%)</td>
<td>1</td>
<td>1</td>
<td>0.52-1.93</td>
</tr>
<tr>
<td>Normal WHR</td>
<td>53(66.2%)</td>
<td>53(66.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family History of</td>
<td>4(5%)</td>
<td>8(10%)</td>
<td>0.369</td>
<td>0.474</td>
<td>0.14-1.64</td>
</tr>
<tr>
<td>Sudden death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Family history of</td>
<td>76(95%)</td>
<td>72(80%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sudden death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>57(71.3%)</td>
<td>59(73.8%)</td>
<td>0.723</td>
<td>0.97</td>
<td>0.440-1.767</td>
</tr>
<tr>
<td>No dyslipidemia</td>
<td>23(26.2%)</td>
<td>23(26.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &gt; 30</td>
<td>18(22.5%)</td>
<td>26(32.5%)</td>
<td>0.157</td>
<td>0.603</td>
<td>0.299-1.218</td>
</tr>
<tr>
<td>BMI&lt;30</td>
<td>62(77.5%)</td>
<td>54(67.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Among the patients with rheumatoid arthritis 64 (80%) were on DMARDS, 49 (77%) were on one DMARD, 14 (21.9%) were on two DMARDS and only one patient with rheumatoid arthritis was on treatment with three DMARDS. None of the patients with RA seen at the clinic were using biological agents for the treatment of rheumatoid arthritis.

Twenty seven patients who used DMARDS were hypertensive as compared to 24 who used no DMARDS. Those who used DMARDS were significantly more likely to have hypertension than those who did not use it OR 2.189(95% C.I 1.111-4.312) P= 0.022. Likewise those patients with RA who used steroids were more likely to be hypertensive than the controls and this was statistically significant OR 2.06(95% C.I 1.008-4.207) P= 0.022. (Table 3)

Table 3: Hypertension in relation to drug therapy in patients with RA and controls

<table>
<thead>
<tr>
<th>Variables/ category</th>
<th>Hypertension n</th>
<th>%</th>
<th>No Hypertension n</th>
<th>%</th>
<th>O.R</th>
<th>95% C.I</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of DMARDS</td>
<td>27</td>
<td>42.2</td>
<td>37</td>
<td>57.8</td>
<td>2.189</td>
<td>1.111-4.312</td>
<td>0.022</td>
</tr>
<tr>
<td>Use of steroids</td>
<td>20</td>
<td>43.5</td>
<td>26</td>
<td>56.5</td>
<td>2.06</td>
<td>1.008-4.207</td>
<td>0.045</td>
</tr>
<tr>
<td>Use of NSAID</td>
<td>13</td>
<td>36.1</td>
<td>23</td>
<td>63.9</td>
<td>1.279</td>
<td>0.586-2.79</td>
<td>0.536</td>
</tr>
</tbody>
</table>

More than half the patients with Rheumatoid arthritis 46(57.5%) were using glucocorticoids. Only one (1.3%) patient with rheumatoid arthritis was on treatment with statins while two (2.5%) controls were using it. Only one (1.3%) patient with RA was using Aspirin (antiplatelet agent) while three (3.8%) in controls were on it. None of the cases or controls were on treatment with nitrates. Eight (24.2) patients who had hypertension and RA were on treatment for hypertension, while three (60%) individuals who had diabetes with RA were on treatment for diabetes.
Thirty (37.5%) patients with RA were taking NSAIDS regularly as compared to six (7.5%) in the control group. Among the individuals with RA taking NSAIDS regularly 12(40%) were hypertensive.

Eleven patients with RA had no cardiovascular risk factors after being evaluated in this study, 20 patients had 1 risk factor, 27 two risk factors, 18 three risk factors and 4 with four risk factors. In the control arm 7 did not have any risk factor, 31 had 1 risk factor, 27 two risk factors, 10 three risk factors, 4 four risk factors and 1 with five risk factors. When the cases and controls were compared there was no statistical significance in terms of number of risk factors.

![Figure 2: Distribution of risk factors by cases and controls](image-url)
CHAPTER 5
5.0 DISCUSSION, CONCLUSION AND RECOMMENDATIONS
5.1: Discussion
Rheumatoid arthritis is a chronic debilitating illness and early diagnosis and initiation of treatment prevents complications from occurring. This is the first study done locally looking on cardiovascular risk factors in patients with RA. From our results we found women were the most affected by the disease accounting for over two thirds of the patients with RA, and less than a third being male patients with RA. Our study population was young with a mean age of patients with RA in our study being 44.7 ±15.3 years. Our results show that hypertension was more common in patients with RA than in the controls and this was statistically significant. Also patients who used NSAIDS had more hypertension than the controls.

A local study done at Kenyatta national hospital recently (Owino MMed dissertation 2007) found the prevalence of women with RA at 86.7% with a male to female ratio of 1:6.5 which agrees with our study. A study done in the UK \(^{19}\) found a prevalence of 73% of patients with RA were women. This was a study carried out on all patients with RA attending routine outpatient clinics in the UK. Although this was a lower prevalence than what we observed in our study it still showed a trend in which rheumatoid arthritis affects women predominantly.

The mean age of our patients with RA was similar to that observed by Oyoo and colleagues in Nairobi \(^{69}\) but older than that observed by Bagg et al \(^{14}\). In the study done in the UK by Panoulas and colleagues \(^{(19)}\) the mean age for patients with RA was 61 ± 12.02 years. This was an older population than what we saw in our study and could explain our higher prevalence of rheumatoid arthritis among women, since the disease has been shown to be more common in younger women compared to younger males; but the difference diminishes as the age increases.

The prevalence of hypertension among the patients with rheumatoid arthritis was higher than in healthy controls. A study done by Panoulas et al \(^{19}\) in the UK found a 70%
prevalence of hypertension in a cohort of patients with rheumatoid arthritis. This population was older than our study population and it has been shown that hypertension is more common in older age group\textsuperscript{20} of individuals.

Antonio \textit{et al} \textsuperscript{6} found a 33% prevalence of HTN in patients with RA in his study. This was a multicentre study and involved different geographical and demographic groups globally but mostly in Europe and North America. This prevalence of hypertension was lower than what we observed in our study despite being an elderly population with a mean age of 57 years; probably the prevalence of hypertension was different in this population.

Use of medium dose steroids for long term (more than six months) in patients with RA has been associated with a high prevalence hypertension \textsuperscript{63}. In our study more than half of patients with RA were on steroids out of which 20 (43.5%) had hypertension. The patients with RA using steroids were twice at risk of being hypertensive than the controls and this was statistically significant. We did not document the daily steroid use in our study and therefore would not have a daily steroid dose to correlate with other studies findings. The use of steroids in patients with RA could also explain the higher prevalence of hypertension in this patient group compared to the controls. A local study done by Owino and colleagues found a 66.7% prevalence of patients with RA on steroids but had a lower prevalence of hypertension than in our study. The use of steroids could not explain the difference in the prevalence of hypertension; probably other factors could explain this observation.

In our study we found almost a quarter of the patients with RA and hypertension were receiving treatment for hypertension, and this shows a significant proportion of patients are not diagnosed with hypertension and therefore could not benefit from early treatment. Panoulas and colleagues \textsuperscript{19} observed that 39.4\% of the individuals with RA were undiagnosed for hypertension and therefore could not get treatment.
In our study a 6.5% prevalence of diabetes was found among patients with rheumatoid arthritis compared to 5% in the control group. Antonio and his colleagues found a 8% prevalence of diabetes in patients with RA in his study. This was a multicentre study and had varied demographic characteristics although 90% of the patients were Caucasians and they had a higher mean age than in our study. Del Rincon et al., found a prevalence of 8.3% of diabetes among patients with RA and 6.3% in his controls, however, this was not statistically significant. This finding in the study done by Del Rincon and colleagues was observed in patients and controls below 55 years of age. He did observe a higher prevalence in those who were above 55 years. The patients in his study were older than in our study and this could explain the higher prevalence he observed in his study or probably the prevalence of diabetes was higher in his study population. Steroids have been shown to predispose patients to diabetes and we may associate the use of it in our study with the higher prevalence of diabetes in patients with RA in our study since over half of them were on steroids.

Almost two thirds of our patients with RA had dyslipidemia with almost a similar number observed in the control group. We have no local data on dyslipidemia among patients with RA. This finding in our study was higher than what was observed by Antonio and his colleagues with a 14% prevalence of dyslipidemia in patients with RA. The low prevalence observed by Antonio and colleagues could have been due to the difference in the cut off levels for lipid profiles. Crowson and colleagues observed a higher prevalence of dyslipidemia in his study of 59.4%. This was a study done in the US looking at risk of developing heart failure attributable to traditional cardiovascular risk factors in patients with RA.

A small proportion of patients with Rheumatoid arthritis in our study were smoking cigarettes, and this trend was also observed in the healthy controls. Lore et al in a local study in Nairobi found 64% of males working at the university of Nairobi and ministry of health employees to be smokers, 7% of those who smoked were females in that study. The low prevalence of smoking in our study might have been influenced by the cultural trends in the Kenyan society. Older women in the Kenyan society tend to be conservative.
and therefore few of them smoke although of late the trend of smoking has been seen to be rising among young women in Kenya. Our findings were in sharp contrast to what was seen in the quest RA study\(^5\) where the prevalence of smoking was at 43% in patients with RA. These could be explained by the population studied in Quest RA study which was more of a western society where a significant proportion of women smoke cigarettes. Panoulas \textit{et al} \(^{19}\) observed a prevalence of 18.5% of smoking in his study and these was still higher than what we saw in our study.

Obesity particularly central obesity is associated with an increased risk of cardiovascular risk \(^{50}\). Antonio and his colleagues in the quest RA study found a prevalence of 18 % and this was lower than what we found in our study. Patients with RA tend present with weight loss when the disease is active and can even loose weight while on treatment and this might explain the difference we got from our study when we compared our patients with RA and the controls.

The number of individuals with RA using DMARDS was 64(80%) in our study. A study done in Nairobi (Owino MMED dissertation 2007) found a 46.7 % prevalence of use of at least one DMARD in patients with RA and this was lower than what we observed in our study. We think that there could have been some improvement in knowledge of the healthcare workers in the use of DMARDS in patients with RA and therefore more people being put on DMARDS now than before. A study done by Panoulas \textit{et al} \(^{19}\) found out that 87.5% of patients with RA were using DMARDS. This was in higher than what we found in our study although the trend was almost similar with over two thirds of our patients with RA using DMARDS.

In our study at least over two thirds of patients with RA were on one DMARD, one fifth on two DMARDS. This was not in agreement to a study done in Europe \(^{19}\) where 56.8% of patients with RA were on only one DMARD. The findings in our study shows a fewer patients with RA were being put on more than one DMARD than what is currently recommended. This finding might reflect on clinical practice at KNH because in other parts of the world rheumatologist are increasingly prescribing combination therapy \(^{56}\).
because single DMARD therapy often fails to control clinical symptoms or prevent disease progression.

The use of NSAIDS especially Cox 2 inhibitors (72) have been associated with hypertension unlike in our study where there was no significant association of hypertension and use of NSAIDS, may be the numbers were small. The use of some DMARDS especially lefluonomide (60) have been associated with hypertension and in our study there was a significant association of hypertension with the use of DMARDS, although the use of single agents was not determined in our study and therefore we could not ascertain the role of lefluonomide in this study.

The family history of documented cardiovascular events was lower than that observed by Crowson et al (85) in the US, there could have been a recall bias among our patients with RA on current disease or their social desirability might have influenced their response. Recording and maintaining updating records of this information in our local set up might have posed a significant challenge and this might explain the low prevalence we got from our study.

Most of the controls in our study were individuals working at the hospital they included the nursing staff, clinical officers and supportive staff, a large proportion of them had dyslipidemia (73.8%) and this was more than in the cases although this was not statistically significant it still shows that this population was at risk. The healthy individuals who were used as controls were also more obese (32.5%) than the patients with RA indicating that they were at more risk although this was not statistically significant. They also documented more family history of sudden death than in the cases with RA. From our findings it seems the control group which was presumed healthy had actually more risk factors than thought and these might have influenced our results especially looking at the lipid profile where we expected to have more dyslipidemia in patients with RA than in the controls as seen in a study done by Situnayake and colleagues (35).
Most of the patients and controls had clustering of risk factors and when the two groups were compared there was no statistical significance between the cases and controls in the clustering of risk factors. The control group which was employees and students doing internship at the hospital seem to have been a risk group in that they also had high cardiovascular risk factors and this may predispose them to more cardiovascular events. May be if we had chosen a general population based group the cardiovascular risk profile may have been different and this may have altered our findings.

5.2 CONCLUSIONS

This study has shown that there is a high prevalence of hypertension in patients with RA as compared to the controls. Hypertension was also associated with the use of DMARDs and steroids.

A large proportion of patients with RA and healthy controls had dyslipidemia.

There was no significant difference between patients and controls in term of other risk factors that is, diabetes mellitus, dyslipidemia, smoking, BMI, WHR, and family history of cardiovascular events.

There was clustering of risk factors among patients and the healthy controls although this was not significant. From our study it seems hypertension may play a role in increasing the risk of cardiovascular events in patients with RA.

5.3 RECOMMENDATIONS

1) Screening for cardiovascular risk factors especially hypertension in patients with RA should be routinely done and preventive strategies promoted especially targeting those at high risk.

2) Patients with RA and on steroid therapy should be closely monitored for high blood pressure and screened for diabetes.

3) A larger study with normal controls from the general population should be undertaken in order to measure cardiovascular risk factors and document the cardiovascular disease in patients with RA.
5.4 STUDY LIMITATIONS

1: Blood pressure measurement- on the spot blood pressure measurement might not be a true reflection of patient’s blood pressure. We needed to rule out “white coat” hypertension. Ideally 2 or more clinic visits was needed to confirm high BP.

2: Recall bias – this occurred when the subject’s recollection of some historical factors was biased based on either their current disease state or social desirability. This might have lead to an under or over - estimation of the significance of a risk factor for example the low prevalence of Tobacco or alcohol use and family history of previous cardiovascular events.

3: Recall bias with regard to symptoms of acute myocardial infarction, patients may not remember having had the symptoms.

4: Selection bias: Those who were enrolled were patients who were only referred to KNH and a significant proportion of sick patients may have been missed out. Since it based on a secondary based cohort, generalisability of results should be cautiously approached.

5: Doing fasting lipid profile was challenging and some patients/controls dropped out after being given a follow up appointment.

6: This was a cross sectional study and has limitations because causality cannot be proven and directionality of associations must be viewed with caution.

7 Our control group was from a hospital workers and it seems they also had a high proportion of cardiovascular risk actors and this might have biased our results. The difference in socioeconomic status might have influenced our findings since most of our controls were employed.
6.0 REFERENCES


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46 Dessein, H.P., Joffe, P.I., and Singh, S. Biomarkers of endothelial dysfunction, cardiovascular risk factors and atherosclerosis in rheumatoid arthritis
Arthritis Res Ther. 2005; 634-43


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APPENDIX 1

STUDY PRO – FORMA DOCUMENT/ QUESTIONNAIRE

Date of Presentation ____________________ Time of Presentation ____________________

1. Personal Data

Patient Name: ________________________

Age ____________________ Sex ________________________

Marital Status [ ] 1 = Married
[ ] 2 = Single
[ ] 3 = Widowed
[ ] 4 = Divorced

Level of formal Education [ ] 1 = Tertiary
[ ] 2 = Primary
[ ] 3 = Secondary
[ ] 4 = College
[ ] 5 = None

Current Status of Employment [ ] 1 = Unemployed
[ ] 2 = Employed
[ ] 3 = Self – Employed
[ ] 4 = Retired

3. Duration of RA Months [ ] Years [ ]

Months [ ] Years [ ]

47
## Symptoms, Signs & Investigation Results Prior to Diagnosis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Yes</th>
<th>No</th>
<th>Duration</th>
<th>Joints Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning Stiffness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis of three or more joints</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis of the hands</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symmetric Arthritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiographic changes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatoid nodules present</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Rheumatoid Factor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Treatment Received

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Regular (YES/NO)</th>
<th>Intermitent</th>
<th>Symptomatic</th>
<th>No Recall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucocorticoid HD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucocorticoid MD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucocorticoid LD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMARDs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSZ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTX</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biologicals (infliximab)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Physiotherapy  Yes  No  regular  intermittent

Occupational therapy  Yes  No  regular  intermittent

Surgery  Yes  No

If yes specify  

Psychiatric treatment  Yes  No

Is currently on treatment for any disease/illness  Yes  No
If yes specify

Diabetes

CHF

Renal failure

Hypertensive  1 = Yes  2 = No  3 = Previously Treated

Others

Any co-morbid conditions or complications of RA on physical exam

6. Other drugs:  

Anti-platelets  1 = Yes  2 = No

Statins  1 = Yes  2 = No

Nitrates  1 = Yes  2 = No

Others  1 = Yes  2 = No

7. Presenting symptoms

8. History of presenting illness

9. Past Medical History
Previous history of chest pain
1 = Yes  2 = No

Previous history of heart attack
1 = Yes  2 = No

Previous history of stroke
1 = Yes  2 = No

Previous history of coronary angiography
1 = Yes  2 = No

Previous history of heart failure
1 = Yes  2 = No

Other
1 = Yes  2 = No

10. Family History:

Parental / Sibling History of RA
1 = Yes  2 = No

Parental / Sibling History of Diabetes
1 = Yes  2 = No

Parental / Sibling History of sudden death
1 = Yes  2 = No

Parental / Sibling History stroke
1 = Yes  2 = No

Parental / Sibling History MI
1 = Yes  2 = No

Other
1 = Yes  2 = No

11. Gynaecological History:
1 = Pre – menopausal  2 = Post – menopausal

12. Social History:

Smoking: Non smoker

Smoker: No. of sticks per day  No. of years  Pack years

Former Smoker: No. of years of abstinence  Pack years:

Alcohol: Never drank alcohol
Drink Alcohol: Type of beverage  
1 = Beer  
No. of Bottles per week
2 = Whisky
3 = Wine
4 = Illicit brews

Former Drinker: Years of abstinence

Physical examination Findings

1. Vital signs: PR [ ] BP 1st [ ] 2nd [ ] Average [ ]
   RR [ ] PR [ ] TEMP [ ]
   Weight [ ] height [ ] BMI [ ]

2. General Examination

3. Waist Circumference [ ] Hip Circumference [ ]
   WHR [ ]

4. Features of heart failure [ ] 1 = Yes 2 = No

5. Other findings
APPENDIX 2

Random blood sugar

Fasting blood sugar

Lab Results

1. Total Cholesterol
   1 = Elevated  2 = Low  Normal

3. HDL Cholesterol
   1 = Elevated  2 = Low  Normal

4. LDL Cholesterol
   1 = Elevated  2 = Low  Normal

5. Triglycerides
   1 = Elevated  2 = Low  Normal
APPENDIX 3

Informed consent explanation

Title of study:
Cardiovascular risk factors in patients with rheumatoid arthritis attending MOPC at Kenyatta National Hospital Nairobi Kenya

Principal investigator: Kirui Fredrick

Participation: Your participation in this study is voluntary. Refusal to participate will involve no penalty to you. You may discontinue participation at any time without any penalty.

Introduction:
We are interested in finding out the burden of high blood pressure and other risk factors to the heart among individuals with Rheumatoid arthritis and compare with those individuals who do not have rheumatoid arthritis. We will measure your blood pressure, your weight, height, waist/Hip circumference. We require 2mls of blood for measuring your blood cholesterol and blood sugar levels.

Procedure to be followed: Upon accepting to participate in this study you will be asked to sign an informed consent after which we will take the history of your present illness, past history of your illness and a doctor will do a physical examination on you. We will also measure your blood pressure and measure your heart beat or rate. Your breathing rate and body temperature. We will take your blood for measurement of fat (cholesterol) and sugar levels in your blood. We will then ask you some questions touching on issues such as; your occupation, income, education level, occupation and current treatment. After doing this we will give you your blood pressure results, your blood fat and sugar level results and accord you appropriate treatment or advice as determined by your results. If you are having any other illness we will refer you to the appropriate clinic to be attended by the doctor at the clinic.
Injury /risk: There is no risk that you will encounter while we measure your blood pressure. You will have a bit of discomfort from the needle prick while we are taking blood for the fat and sugar levels.

Benefits: You will benefit from free consultation, free blood fat levels and a free blood sugar check.

Duration of participation: We require at most 2 hours so as to be able to get the results of blood pressure and take blood for fat and sugar level measurement and offer you the necessary treatment or advice depending on the outcome of the tests.

Who can participate in this study: A person above 18 years who has been confirmed to have RA as per ACR criteria and is willing to sign an informed consent. Also those who do not have rheumatoid arthritis will be recruited.

Assurance of confidentiality of volunteer’s identity: Records relating to your participation in the study will remain confidential. Your name will not be used in any report resulting from this study. All computerized and laboratory specimens will contain only a unique study number.

Subject: If during the course of this study you have any questions concerning nature of research you should contact Dr Fredrick K Kirui P.0 Box 3249-00200 Nairobi Kenya Telephone no 0202722541/0723543111.

CONSENT FORM

I ................................................ being a person 18 years and over do hereby give consent/permission to Dr /Mr. /Ms ......................to include and carry research on me in the intended research protocol. I have read and understood the contents of this form. I do also understand that at any time of the study I may revoke my consent and withdraw my self from the study without prejudice. This has been explained to me in a language that I do understand.

Volunteer name .......................................Signature Date
If you have any questions to ask any other person not involved in these study, you may contact.

Chairman Kenyatta National Hospital Ethical Review Committee
APPENDIX 4

MAELEZO YA FOMU YA MAKUBALIANO

MADA
Cardiovascular risk factors in patients with Rheumatoid arthritis attending MOPC at Kenyatta National Hospital Nairobi Kenya

Mchunguzi mkuu
Kirui Fredrick Kipkorir

Kushiriki
Usajili na kushiriki ni hiari. Kugoma kushiriki au kujiondoa kutoka kwenye uchunguzi huu hakutashirikisha adhabu ama kupotea kwa haki ulizokusudiwa.

Maelezo ya mwanzo
Tuna haja ya kujua idadi ya watu wenye kipimo ya pressure ya damu iliyoko juu kuliko kawaida na madhara mengene ya monyoo katika watu wanayo kuwa na ugonjwa wa viungo inayoitwa rheumatoid arthritis na pia wenye hawana ugonjwa huu wa rheumatoid arthritis. Tuta pima pressure yako ya damu, Uzani wa mwili wako, urefu wako na kuchukuwa damu yako ili tupime mafuta ya cholesterol na sukari katika damu yako.

M pangilio utakayofuatwa
Ukipatikana na magonjwa mengini utapewa mwelekeo mwafaka na kisha kutumwa kwenye kliniki zinazofaa.

Madhara/hatari
Hakuna hatari yeyote wakati unapotupa damu yako. Madhara utakayo pata tukichukuwa damu ni uchugu wa sindano ambayo hautakuwa mwingi. Hizi madara haidhuru sana mwili na endapo uchungu utazidi utapewa matibabu sawasawa.

Faida
Utafaidika kwa kuwa tuta pima pressure ya damu, mafuta na sukari katika damu yako bila malipo yeyote na kukupa ushauri kulingana na majibu tutakayo pata bila malipo yeyote.

Muuda wa kushiriki
Tutahitaji masaa mawili ili tupime damu yako na kukupa matibabu kulingana na majibu.

Nani anaweza kushiriki katika hili uchunguzi
Mtuu yeyeote anayekuwa na miaka 18 na kwenda juu ambaye amepatikana ana ugonjwa wa rheumatoid arthritis kulingana na criteria ya ACR na mwenye kubali kuhusishwa kwenye hili utafiti.

Hakikisho ya siri ya muhusika katika utafiti.
Chochote utakachomwambia msaili wetu, matokeo ya uchunguzi katika kliniki aidha matokeo ya maabara yatakuwa siri na yatatumika tu kwa minajili ya uchunguzi pekee. Damu yako itaharibiwa baadha ya utafifiti kukamilika.

Mhusika.

Ukiwa na maswali au dukuduku lolote kwenye hatua yoyote ya uchunguzi na ungependa kuuliza, tafadhali jihisi huru kufanya hivyo. Una wesa kuwasiliana na Dkt Fredrick K Kirui P.0 Box 3249-00200 Nairobi Kenya. Nambari ya simu 0202722541 Simu ya Mkono 0723543111.
FOMU YA MAKUBALIANO

Mimi .................................................................muhusika na nina miaka 18 na kuelekea juu ,kwa hiari natoa ithibati ya kushiriki kwenye uchunguzi huu kwa Dkt /Mr. /Ms.................................................................................................................................


Jina la muhusika.................................Sahihi ........................................Tarehe

Jina la mchumguzi.................................Sahihi ........................................Tarehe.

Na ukitaka kuuliza chochote mtu mwengine asiyehusika na utafiti huu tafadhali wasiliana na Chairman Kenyatta National Hospital Ethical Review Committee.
APPENDIX 5
The 1987 ACR revised criteria for the classification of rheumatoid arthritis

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Morning stiffness</td>
<td>Morning stiffness in and around joints, lasting at least 1 hour before maximal improvement.</td>
</tr>
<tr>
<td>2. Arthritis of 3 or more joint areas</td>
<td>At least 3 joint areas simultaneously have had soft tissue swelling or fluid (not bony overgrowth alone) observed by a physician. The 14 possible areas are right or left PIP, MCP, wrist, elbow, knee, ankle, and MTP joints.</td>
</tr>
<tr>
<td>3. Arthritis of hand joints</td>
<td>At least one area swollen (as defined above) in wrist, MCP, or PIP</td>
</tr>
<tr>
<td>4. Symmetric arthritis</td>
<td>Simultaneous involvement of same joint areas (as defined in 2) on both sides of the body (bilateral involvement of PIP, MCP, or MTPs is acceptable without absolute symmetry)</td>
</tr>
<tr>
<td>5. Rheumatoid nodules</td>
<td>Subcutaneous nodules, over bony prominence, or extensor surface, or juxta-articular regions, observed by a physician.</td>
</tr>
<tr>
<td>6. Serum rheumatoid factor</td>
<td>Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in &lt;5% of normal control subjects.</td>
</tr>
<tr>
<td>7. Radiographic changes</td>
<td>Radiographic changes typical of rheumatoid arthritis on posterior anterior hand and wrist radiographs which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (osteoarthritis changes alone do not qualify)</td>
</tr>
</tbody>
</table>

For classification purposes a patient shall be said to have rheumatoid arthritis if he/she has satisfied at least 4 of these 7 criteria. Criteria 1 through 4 must have been present for at least 6 weeks. Patients with 2 clinical diagnoses are not excluded.
APPENDIX 6

The International Classification of adult underweight, overweight and obesity according to BMI (WHO)

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Principal cut-off points</th>
<th>Additional cut-off points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.50</td>
<td>&lt;18.50</td>
</tr>
<tr>
<td>Severe thinness</td>
<td>&lt;16.00</td>
<td>&lt;16.00</td>
</tr>
<tr>
<td>Moderate thinness</td>
<td>16.00 - 16.99</td>
<td>16.00 - 16.99</td>
</tr>
<tr>
<td>Mild thinness</td>
<td>Classification</td>
<td>17.00 - 18.49</td>
</tr>
<tr>
<td>Normal range</td>
<td>18.50 - 24.99</td>
<td>18.50 - 22.99</td>
</tr>
<tr>
<td></td>
<td></td>
<td>23.00 - 24.99</td>
</tr>
<tr>
<td>Overweight</td>
<td>≥25.00</td>
<td>≥25.00</td>
</tr>
<tr>
<td>Pre-obese</td>
<td>25.00 - 29.99</td>
<td>25.00 - 27.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27.50 - 29.99</td>
</tr>
<tr>
<td>Obese</td>
<td>≥30.00</td>
<td>≥30.00</td>
</tr>
<tr>
<td>Obese class I</td>
<td>30.00 - 34.99</td>
<td>30.00 - 32.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>32.50 - 34.99</td>
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<tr>
<td>Obese class II</td>
<td>35.00 - 39.99</td>
<td>35.00 - 37.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>37.50 - 39.99</td>
</tr>
<tr>
<td>Obese class III</td>
<td>≥40.00</td>
<td>≥40.00</td>
</tr>
</tbody>
</table>
Adult Treatment Panel III or (ATP III) guidelines. For management of serum lipids

- Serum LDL Cholesterol > 2.58mmol/L (< 100 mg/dl) - Optimal
- Serum LDL Cholesterol > 2.58-3.34mmol/L (100-129mg/dl) - Near optimal
- Serum LDL Cholesterol > 4.12-4.90 (160-189 mg/dl) - High
- Serum LDL Cholesterol > 4.90 (>190mg/dl) - Very high

- Serum HDL Cholesterol <1.03mmol/L (< 40 mg/dl) - Low
- Serum HDL Cholesterol >1.6mmol/L (>60 mg/dl) - High

- Serum Total Cholesterol < 5.17mmol/L (> 200mg/dl) - Desirable Serum Total
- Cholesterol > 5.17-6.19 mmol/L (200-239mg/dl) - Borderline high
- Serum Total Cholesterol > 6.19 mmol/L (>240mg/dl) - High

- Serum Triglycerides > 1.69mmol/L (<150mg/dl) - Normal triglycerides
- Serum Triglycerides 1.69-2.25mmol/L (150-199mg/dl) - Borderline high
- Serum Triglycerides 2.26-5.63mmol (200-499mg/dl) - High triglycerides
- Serum Triglycerides >5.63 (>500mg/dl) - Very high