RHEUMATOID ARTHRITIS AT KENYATTA NATIONAL HOSPITAL:
A CLINICAL AND QUALITY OF LIFE EVALUATION.
A DISSERTATION PRESENTED IN PART FULFILMENT FOR
THE DEGREE OF MASTERS OF MEDICINE [INTERNAL
MEDICINE] OF THE UNIVERSITY OF NAIROBI.

BY:

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Declaration:

I certify that this dissertation is my own original work, and that it has not been submitted by any other person for purposes of a degree in any other university.

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DEDICATION

To the alleviation of pain and suffering, and the improvement of Quality Of Life in patients with rheumatoid arthritis.
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LIST OF ABBREVIATIONS

1. ACR------ American College of Rheumatologists.
2. ANA------ Antinuclear antibody.
3. ANOVA---- Analysis of variance.
4. Anti-CCP---- Antibodies to cyclic citrullinated peptide.
5. ARA----- American Rheumatic Association.
6. CRH------ Corticotrophin releasing hormone.
7. CRP------ C-reactive protein.
8. CT-------- Computerized tomography.
9. DAS------ Disease activity score.
11. DEXA ------- Dual emission X-ray absorptiometry.
12. DMARD ----Disease modifying anti-rheumatic drugs.
13. ENA-78 ------ Epithelial neutrophil activating peptide 78.
14. ESR ------- Erythrocyte sedimentation rate.
15. FBC ----- Full blood count.
17. HAQ ------ Health Assessment Questionnaire.
18. HBGF ----- Heparin binding growth factor.
19. HCQ ------ Hydroxy-chloroquine.
20. HRQOL ------ Health related quality of life patient questionnaires.
21. ICAM ------ Intracellular adhesion molecules.
22. IFN ------- Interferon.
23. IL -------- Interleukin.
24. KNH ------ Kenyatta National Hospital.
25. MAF ------ Macrophage angiogenic factor.
26. MCP ------ Macrophage chemotactic protein.
27. MRI ------ Magnetic resonance imaging.
28. MTX ------ Methotrexate.
29. NO --------- Nitric oxide.
30. NSAID ------ Non-steroidal anti-inflammatory drugs.
31. OA --------- Osteo-arthritis.
32. PAF -------- Platelet activating factor.
33. PG --------- Prostaglandin.
34. QOL ------- Quality of life.
35. RA --------- Rheumatoid arthritis.
36. RF -------- Rheumatoid factor.
37. SF-36 ------ Short Form-36, a generic questionnaire for assessing HRQOL.
38. SLE -------- Systemic lupus erythematosus.
39. SSZ ------- Sulfasalazine.
40. TGF ------ Transforming growth factor.
41. TNF ------- Tumor necrosis factor.
42. VCAM ----- Vascular cell adhesion molecule.
43. VEGF ------ Vascular endothelial growth factor.
44. PCSS ------ Physical component summary scores.
45. MCSS ------ Mental component summary scores.
46. HTN-------- Hypertension.
47. PUD-------- Peptic ulcer disease.
48. HHD ------ Hypertensive heart disease.
49. DM -------- Diabetes mellitus.
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1. Appendix I --------------------- ACR Criteria for the classification and diagnosis of RA.

2. Appendix II ---------------------- SF-36

3. Appendix III --------------------- Patient questionnaire.

4. Appendix IV ---------------------- Explanation and consent form.
ABSTRACT

OBJECTIVES:
To determine the socio-demographic, clinical and QOL profiles of patients with RA at KNH.

STUDY DESIGN:
This is was a cross-sectional descriptive study.

STUDY SITE:
The study was conducted on patients attending the medical outpatient clinic at KNH.

RESULTS

Sixty of the 180 patients screened satisfied the inclusion criteria and were recruited for the study. Of the 60 patients, 8 were male and 52 female [M: F = 1: 6.5]. Mean age of patients was 41.38 ± 16.78. The mean duration, in months, of rheumatoid arthritis was 64.97 ± 85.02 with both mode and median duration of 24 months [range was 1 to 300 months]. The proportion of patients with level of education of primary school and below was 51.7%, while primary together with secondary level education accounted for the highest figure of 68.3%. A large majority of the patients [70.2%] were unemployed.

In 75% of the study patients, one or more of the metacarpophalangeal and proximal interphalangeal joints of the hand were involved by RA. Other frequently involved sites include wrists, elbows, knees, ankles and gleno-humeral joints of the shoulders. Serum rheumatoid factor was positive in 78.9%, while rheumatoid nodules were present in 13.3% of the study patients. A large majority of patients [88%] had active disease, with mild disease accounting for 18%, moderate disease 38% and severe disease 32%. The remaining 12% of the patients had inactive disease [remission].

Fifty-eight percent of study patients had physical component QOL scores ranging from poor to fair compared to sixty-five percent who had mental component QOL scores ranging from good to very good.
46.7% of the study patients were on treatment with at least one DMARD from a selection of MTX, SSZ, HCQ and the biologic leflunomide, while the most frequent drug combination was MTX plus prednisone in 30% of study patients. 66.7% were on oral prednisone while 25% took only non-steroidal anti-inflammatory drugs.

CONCLUSIONS:
A large majority of the patients had active disease, most of them with moderate to severe disease. Less than half of the patients were on DMARDs, a significant number were on NSAIDs alone, while the majority was on prednisone. Physical component QOL ranged from poor to fair, while mental component QOL ranged from good to very good in the majority of patients. Most of the patients were female, young, unemployed, with low level of education.

RECOMMENDATIONS
There is an urgent need to implement appropriate treatment guidelines in order to get majority of our patients into early disease remission. There is need to conduct a comparative QOL study using the same SF-36 version on patients with a different disease entity. There is a need to conduct a study on the effects of co-morbidity on QOL of patients with RA.
INTRODUCTION AND LITERATURE REVIEW.

The first clinical description of RA in medical literature is generally attributed to Landre-Beauvais in his thesis titled Goutte Asthenique Primitive published in Paris in the year 1800 [1]. The term rheumatoid arthritis was however coined by Garrod in 1859, and subsequently used widely for all forms of chronic inflammatory polyarthritis of peripheral joints [1]. Waaler in 1940 and Rose et al 1948 discovered rheumatoid factor [1]. Miall, in 1955, was the first to propose a diagnostic criteria for rheumatoid arthritis for epidemiologic surveys [1]. The criteria was based on three orders of data: - Clinical, radiological and serological i.e. cases with painful joint swellings of hands and feet, who also had either x-ray evidence of erosive changes in joints of extremities, or rheumatoid factor demonstrated. In 1956, committee of the ARA formulated criteria for defining RA in clinical practice [1]. These have since been revised [in 1987] into the current ACR criteria for the classification of RA [2].

DEFINITION OF RHEUMATOID ARTHRITIS.

RA is a chronic systemic autoimmune inflammatory disorder 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 the 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. These include anaemia, splenomegally, weight loss, vasculitis, serositis, mononeuritis multiplex, interstitial inflammation in the lungs and exocrine salivary and lacrimal glands, as well as nodules in Subcutaneous, pulmonary and scleral tissue [3].

See appendix 1 for the American Rheumatic Association 1987 revised criteria for the classification of RA.
EPIDEMIOLOGY:
Criteria and methods for diagnosis of RA have varied in different epidemiological studies. Some have been based on retrospective analysis of hospital records and others on prospective observations of patients attending hospitals where clinical examination, rheumatoid factor tests and radiography have been employed. Questionnaires with or without clinical examination, with or without tests for rheumatoid factor and radiography have also been used in population studies. However, in recent years, there has been a tendency towards a more widespread use of ACR criteria thus introducing a measure of standardization [3].
RA is observed throughout the world and affects all races. Women are affected approximately three times more often than men but this difference diminishes in older age groups. Although RA can occur at any age the incidence increases with advancing age, peaking between ages 40 to 60 years [4].
The incidence of RA in the US and Europe, from a recent study, stood at 54/100,000 in women and 24.5/100,000 in men [3]. The prevalence of RA in the general population in Europe and the US is between 0.8 and 1.1 percent from cross-sectional studies [3]. A strikingly high prevalence rate of 4 to 5 percent has been noted among some native American populations, for example the Pima and Chippewa Indians [3]. Lower prevalence of 0.2 to 0.3 percent has been reported in China and Japan [3]. The prevalence of RA amongst black population is low in rural South Africa [approx 0.2 percent] whereas prevalence rates of almost 1 percent have been observed among black populations in urban black South Africans and in the USA [3].
Some studies have reported virtual nonexistence of RA in parts of Nigeria, while a low incidence has generally been reported in west Africa compared to other parts of the world [3].

There has been a changing pattern in prevalence and severity of RA in the rest of Africa though. Earlier studies suggested that RA was a rarity in sub-Saharan Africa [5]. Gelfand, in 1957, rarely saw it in central Africa [6], and reports from Malawi by Goodal, in 1956 [7], from Uganda by Shaper and Shaper in 1958 [8], and from Nigeria by Greenwood in 1969 [9], have suggested that it is not an important cause of admission to hospital in these countries. In Kenya a single case of nodular RA, seen in Nairobi in 1962, was thought sufficiently unusual to merit a report [10] and, in a retrospective analysis of 26,000 admissions to the Kenyatta National hospital, only 5 cases were found [11].

The earlier reports from Mulago Hospital in Kampala have been followed by progressively larger series, with 65 cases of RA described by Kanyerezi in 1970 [12], and a review of no less than 404 patients with classical RA by Kanyerezi in 1980 [13], the largest series by far to come out of Africa, and in which many cases of severe and sero-positive disease, with the usual range of extra-articular manifestations and much disability were reported unlike the mild and rare disease of earlier reports [5]. An exception may be Nigeria where the disease has appeared to remain mild and uncommon [14].

In view of a clinical impression that increasing numbers of cases of RA were being seen at Kenyatta National Hospital, a prospective study involving 76 patients who fulfilled ARA criteria for RA was carried out by Bagg et al in 1979 [15]. In terms of age, sex, pattern of joint involvement, and nodularity, these patients more closely resembled their European counterparts than they did those described in West Africa by Greenwood in 1969 [9], and in rural South Africa by Beighton et al in 1975 [16], where a male preponderance has been reported and rheumatoid nodules would appear to be uncommon.
There was, however, a striking absence of the systemic nonarticular complications of RA, and few patients showed the more severe degrees of disability at presentation.

The severity of radiological changes seen in the Kenyan patients more closely resembles that seen in an English study by Thould and Simon in 1966 [17], than that reported in Nigerians. However black Zimbabweans with RA seem to have disease that is clinically and radiologically less severe when compared to UK white patients [18, 19].

In another study carried out in Kenya by V. Houba et al in 1979 [20], sera from 48 Kenyan Africans with RA, 43 patients with other diseases, and 98 blood donors were tested for the presence of rheumatoid factor by various latex fixation tests. In the patients with RA the frequency of rheumatoid factor was comparable to that reported in series from Europe and the U. S. A. In the control patients and blood donors a high frequency of positive tests for rheumatoid factor was found; a similar result has been found from population studies in other African countries [20].

AETIOLOGY OF RA.

The initiating cause of RA remains unknown. The following factors have been shown to play a role though [21, 3]:

Genetic factors: Concordance rates for monozygotic and dizygotic twins from studies in western populations strongly favour multigenic influence and argue for an environmental trigger.

An association with allelic polymorphisms of genes on long arm of chromosome 6 [some subtypes of HLA DR4 and HLA DR1] has been shown. These 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 [3].
Environmental factors: cigarette smoking has been associated with increased risk of RA in two prospective population studies and one twin study. Other environmental factors implicated, for example viruses, have proven to be largely speculative while other linkage studies have shown largely conflicting results [3].

Host factors: Observations implicate sex hormones and prolactin in susceptibility or protection in RA, for example [3]:

RA is commoner in females, especially premenopausals, than in males.
Contraceptive pill confers protection by delaying onset of RA.
RA is suppressed during pregnancy.
Incidence of RA increases during post-partum period and during lactation.
Testosterone levels are reportedly low in males with RA and the incidence of RA increases with advancing age when male sex hormone levels fall.

PATHOLOGY AND PATHOGENESIS OF RA:

Pathology of joint disease: The rheumatoid disease process in the joint is characterized by synovitis, an inflammatory effusion and cellular exudate into the joint space, and by damage to tendons, ligaments, cartilage, and bone in and around articulating surfaces of the joint. Long tendons whose sheaths are lined by synovial membrane, such as in the palms, wrists, ankles, and feet, may also be involved by the inflammatory process and cause malfunction due to damage, rupture, and fibrosis.

In health the synovial membrane [the intima] is a film of one or two cells lining the capsule and its circumferential attachment to the periosteum at the cartilage-bone junction. The normal intima consists of macrophage-like cells and fibroblast-like synoviocytes [3].

In established RA the synovial membrane typically becomes enormously thickened [2 to 10 cell layers] and assumes a villous appearance with the macrophage-like cells predominating.

The sublining layer [subintima] is also greatly expanded by newly formed blood vessels and infiltrating mononuclear cells, including T lymphocytes, lymphoblasts, B cells, plasma cells, monocytes, macrophages, dendritic cells, and synoviocytes. The cellular
infiltrate usually has a recognizable architecture, comprising perivascular aggregates of CD4+ T cells. Cells in the interaggregate areas include macrophages expressing HLA class II, CD8+ T cells, activated B cells, dendritic cells, and plasma cells [3].

The intimal surface is bathed in an inflammatory synovial fluid containing a predominance of polymorphonuclear cells but also rich in pro-inflammatory cytokines and immune complexes containing rheumatoid factor. It is also a site of local complement consumption.

The destructive lesion in the joint typically occurs at the circumferential attachment of the joint capsule, just below and adjacent to the articular cartilage and subchondral bone. Here the intima of adjacent hypertrophic synovial membrane creeps over the cartilage, and tissue rich in blood vessels, macrophages, osteoclasts, and synoviocytes [termed pannus] invades and destroys variable parts of articular cartilage and subchondral bone. A number of enzymes responsible for degradation of cartilage matrix have been demonstrated in the rheumatoid joint, including matrix metalloproteinases I, III, and XIII, cathepsins and collagenases [3].

Pathology of extra-articular disease: This comprises essentially two types of lesions. The first involves arterial walls with two types of pathologies described. The first type of pathology is a bland fibro-intimal hyperplasia, without obvious inflammatory changes, resulting in vascular occlusion. This pathology is typically observed in digital vessels in longstanding disease, is associated with collateral vessel formation, and intermittent nail-fold infarcts. The second type of pathology is polyarteritic, observed in rheumatoid systemic vasculitis, and of poor prognosis involving medium and small-sized arteries of the limbs, peripheral nerves, and organs but sparing renal vessels.

The second type of lesion leads to extravascular lymphocyte-macrophage granuloma formation. Extravascular nodule formation in areas subject to pressure or friction is the characteristic granulomatous lesion of RA. Extravascular granuloma, with or without nodules, may occur on pleura, pericardium, and endocardial valves [3].
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Pathogenesis:

The first event in RA is probably antigen-dependent activation of T cells, which subsequently leads to multiple effects including activation and proliferation of synovial lining and endothelial cells, recruitment and activation of additional proinflammatory cells from the bone marrow and circulation, secretion of cytokines and proteases by macrophages and fibroblast-like synoviocytes, and autoantibody production [Fig. 1].

Fig. 1: Aetio-pathogenesis of rheumatoid arthritis.
**T lymphocytes**- The activation of T cells, due to as yet unknown antigens, in the immunogenetically susceptible host is most probably the first event that initiates the rheumatoid process. T cells constitute about 50% or more of cells in most rheumatoid synovia; most of these are CD4+ but only 5% or fewer are B lymphocytes or plasma cells. CD4+ T cells provide B cell help that can potentially increase synovial antibody production. One observation is that, in RA, there appears to be a pre-selection of high affinity, self-reactive T cells in the thymus. On arriving in synovium these may be presented with self-antigens [e.g., gp39] and be activated, initiating the inflammatory response [21].

**Autoantigen[s] and T cell proliferation**- Once the immune response is triggered by the inciting antigen[s], additional antigens also recognized by T cells may contribute to an ongoing response.

Such candidate antigens include:

1. **Type II collagen**, which is uniquely found in articular cartilage and the vitreous of the eye.

2. **Cartilage antigen gp39**, secreted by both synovial cells and chondrocytes, and is selectively induced at sites of inflammation and tissue injury.

3. **Citrullinated peptides**- Anti-CCP antibody is present in the earliest stages of disease in almost 70% of RA patients.

4. **Glucose 6 phosphate isomerase** [21].

**B lymphocytes**- Studies have demonstrated that the depletion of peripheral blood B cells with an anti-CD20 antibody in patients with autoimmune diseases, including RA, reduces disease activity despite the fact that serum immunoglobulin levels remain unchanged. This observation supports the proposition that B cells have an antibody-independent role in the pathogenesis of RA and systemic autoimmunity in general. Although their precise role is not clear, there are several mechanisms that could profoundly influence the disease process [22, 23].
B cells may function as antigen-presenting cells and provide important costimulatory signals required for CD4+ T-cell clonal expansion and effector functions. In addition, it is known that the synovial membrane in patients with RA contains an abundance of plasma cells [derived from B cells] that produce rheumatoid factor and that positivity for rheumatoid factor is associated with more aggressive articular disease, a higher frequency of extra-articular manifestations, and increased mortality. Immune complexes that contain rheumatoid factor bind to Fc receptors on macrophages in the synovial membrane, inducing the release of pro-inflammatory cytokines, such as tumor necrosis factor alpha. Rheumatoid factor may also be a self-perpetuating stimulus for B cells, potentially leading to activation of and antigen presentation to T helper cells, which could be mechanistically responsible for further production of rheumatoid factor. Finally, although T cell activation is considered to be a key component of pathogenesis of RA, recent evidence indicates that such activation depends on the presence of B cells [23].

Pathogenesis of rheumatoid synovitis- For unknown reasons, the embryonic immune response in RA is centered within the synovium. One of the earliest pathologic responses in RA is the generation of new synovial blood vessels. In the mature rheumatoid synovium, the mass of tissue is too much for even the multiple new capillaries to nourish, and local tissue ischaemia results. Relative synovial hypoxia is associated with an increased production of angiogenic cytokines such as VEGF and the VEGF receptor, HBGF, MAF, PG-E1, PG-E2, IL-8, ENA-78, and angiopoietin-1. TNF-alpha also indirectly stimulates angiogenesis by upregulating the production of angiopoietin-1 and its receptor, and VEGF. Without new blood vessels, there would be no scaffold upon which synovitis would grow. RA can therefore be considered angiogenesis-dependent disease. Balancing this angiogenic response are factors which tend to inhibit neovascularization. These include interferon-gamma [IFN-g], TGF-beta, IL-1, angiostatin, endostatin, and low molecular weight substances in articular cartilage. Some of the standard drugs used in the past to manage RA, e.g. D-penicillamine and gold salts, may also have anti-angiogenic qualities [21].
IL-15, produced by macrophages, can induce TNF-alpha production through activation of synovial T cells in RA.

IL-17, produced by T cells, enhances IL-6 production and collagen destruction. It also increases bone resorption by enhancing osteoclast activation and decreased bone formation.

IL-18 helps sustain the Th-1 phenotype associated with RA and promotes the production of pro-inflammatory cytokines, including TNF-alpha and IL-1 beta. Expression of IL-18 in synovial tissue in RA correlates with acute phase response.

TGF-beta, a reparative cytokine, inhibits T cell activation and proliferation, down-regulates B cell proliferation and differentiation, inhibits biosynthesis of metalloproteinases, protects articular cartilage from the degradative influences of IL-1, inhibits TNF-alpha secretion by macrophages, and accelerates wound repair. As yet however there have been no therapeutic trials of recombinant TGF-beta in RA patients in part because active TGF-beta, in contrast to the latent form, has a very short half life in vivo (21).

The hypothesis that TNF-alpha is a dominant inflammatory mediator in the cytokine dysequilibrium observed in the rheumatoid synovium has gained considerable support. In particular, TNF-alpha regulates production of IL-1 and together these two cytokines orchestrate rheumatoid inflammation and damage (3). TNF-alpha also drives the production of IL-6, IFN-g, and substance P (21). Use of biological inhibitors of TNF-alpha in RA has shown TNF-alpha to be responsible in the following ways:

1. It is responsible, through chemotactic cytokine production e.g. IL-8, MCP-1, and induction of expression of vascular adhesion molecules such as ICAM-1, E-selectin, and VCAM-1, for migration and retention of various inflammatory cells in the rheumatoid synovium.

2. Together with IL-1, it is responsible for activation of osteoclasts in the pannus tip involved in bone erosions, and for the activation of macrophages and synoviocytes at capsule-cartilage junction involved in destruction of articular cartilage.
3. It stimulates the production of matrix metalloproteinase I, III, XIII and other collagenases which degrade collagen in cartilage, bone, and tendon.

4. It causes raised levels of CRP, ESR, and serum amyloid A protein.

5. Together with IL-1 and IL-6 they cause the systemic manifestations of RA such as malaise, fever, weight loss and fatigue [3].

Most of the other effects of TNF-alpha have already been mentioned in earlier paragraphs of this chapter.

Development of synovitis in synovial fluid: The manifestations here are different from those in the synovium. The abnormal physiology induced by the accumulation of fluids also has toxic effects. In very active disease, up to one billion polymorphonuclear leucocytes may gain access to a rheumatoid knee joint each day, while few if any leave the joint and are degraded. These cells subsequently deposit gene products and contents of granules [azurophil, specific, and C] in the synovial fluid. These include myeloperoxidases, Elastases, lysozyme, collagenase, acid hydrolases, matrix metalloproteinases, IL-1 beta, prostaglandins, PAF, and leucotrienes. These products once released into the synovial fluid can cause considerable damage. In addition, since leucotriene B4 and PAF are among the most potent chemoattractants known, activated neutrophils are able to recruit additional neutrophils in an autocrine fashion. Activated leucocytes also produce oxygen-derived free radicals which are very damaging [21].

Compliment activation and immune complexes: Activated complement components have intrinsic inflammatory activity. Activated compliment often indicates the presence in tissues of immune complexes of sufficient size to independently activate the entire system. Immune complexes can also generate secondary antibody responses towards T cell-dependent antigens, and activate memory B cells and plasma cells. C3a, or anaphylatoxin, is a product of C3 activation which increases capillary permeability. C3a is inactivated by an enzyme that cleaves its terminal arginine residue [C3adesArg]. Levels of both C3a and C3adesArg are elevated in rheumatoid synovial fluid; furthermore, the levels correlate with C-reactive protein [CRP] levels, ESR, and disease activity indices.
The deposition of rheumatoid factor IgG complexes along with complement in superficial layers of articular cartilage may be a major force in attracting invasive synovial cells into cartilage [21].

Nonimmune factors: Additional factors, including NO, neuropeptides, and arachidonic acid metabolites, may contribute in the pathogenesis of RA. NO has a less well-defined role in inflammatory states, but whether toxic or anti-inflammatory, NO is produced by patients with RA in greater amounts than in controls. A neuropeptide fibroblast like substance P can activate macrophages, stimulate B cell differentiation, cause proliferation, attract neutrophils, and increase expression of cytokines, prostaglandins, and metalloproteinases. CRH may play a local, pro-inflammatory role in rheumatoid synovium. Higher concentrations of CRH are found in synovial fluid of patients with RA compared to those with OA and a higher density of CRH receptors in synovium is also present in those with RA.

The arachidonic acid metabolites, especially PG-E2, play a major role in RA by stimulating periarticular bone resorption early in disease, and by enhancing the manifestations of acute joint inflammation like pain, increased vascular permeability, and potentiating inflammatory effects of other mediators. Factors responsible for clotting and fibrinolysis may have a role in RA. Thrombin is mitogenic for synovial cells, has angiogenic properties, enhances endothelial adhesion molecules and arachidonic acid synthesis and promotes platelet aggregation. Fibrin itself may promote cell growth and adhesion within the synovial pannus. Serine proteases that are mediators of fibrinolysis, including plasminogen activators and plasmin, may also contribute to cartilage degradation [21].

CLINICAL FEATURES OF RA:
The onset of RA is frequently insidious and the principal symptoms are pain and stiffness, mainly of peripheral joints, with associated pain, swelling, and tenderness. Prolonged stiffness of joints on waking and following inactivity is usual and may last for an hour or more.
There is progressive decline in physical function and ability to perform daily activities. Fatigue and lethargy are common and there may also be low-grade fever and weight loss. As the disease evolves, further joints may become involved and some may remit, but ultimately the distribution of arthritis becomes permanently established [3].

Other patterns of disease presentation are also recognized. Up to one third of patients present with explosive or subacute onset of arthritis, leading to severe immobility. In a minority of patients a migratory poly-arthritis is observed. About 10% of patients present with features of polymyalgia rheumatica, characterized by prominent limb-girdle pain, stiffness, and painful movement of the neck, shoulder, and hips. Persistent inflammatory arthritis of a single joint such as the knee, ankle, wrist, shoulder, or hip may be the only rheumatological symptom and can antedate the onset of polyarthritis by months or years. The expression of RA shows inter-individual variation with respect to the anatomical sites and numbers of involved joints. In 80 to 90% of patients, one or more of the metacarpophalangeal and proximal interphalangeal joints of the hand and the metatarsophalangeal joints are involved. Symmetrical involvement of the joints is usual, but there may be exceptions. Rarely, the initial manifestations of RA are confined to extra-articular disease. Examples include Nodules, systemic vasculitis, fibrosing alveolitis and obliterative bronchitis, serositis, eye complications [scleritis, episcleritis, scleromalacia perforans, corneal melt, and keratoconjunctivitis sicca.], amyloidosis, osteoporosis, Feltys syndrome, myocardial disease, neurological complications [compression and peripheral neuropathies], and increased susceptibility to infections [3].

LABORATORY TESTS:
Laboratory studies are an integral part of management of patients with RA and are employed for diagnosis, evaluation of prognosis, assessment of disease activity, response to therapy, and monitoring toxic effects of drugs. Routine tests include:

1. IgM RF, better done by Rose-Waaler method, a positive result is one that exceeds titres observed in less than 5% of normal controls, or the value set by an international reference standard, and is observed in 70% of patients at some point in their disease
course. It is moderately specific for RA but can also be observed in other connective tissue diseases such as SLE and Sjogren's syndrome.

A repeat test may be positive after an initial negative result and is therefore necessary before a patient is categorized as seronegative RA. A significant titre of rheumatoid factor is associated with a poor prognosis and extra-articular disease.

1. ESR, measured by Westergreen method, and serum CRP levels correlate with disease severity.
2. FBC: A high level of disease activity is associated with a normocytic normochromic anemia, polymorphonuclear leucocytosis, and thrombocytosis. These abnormal values tend to return to normal as the inflammatory component responds to therapy.
3. Liver and renal function tests: Useful especially in monitoring for toxic effects of the commonly used drugs, methotrexate and nonsteroidal anti-inflammatory drugs.

Currently there are other laboratory tests, which are not routine though, such as:
1. Serum sE-Selectin level has currently been identified as the best parameter available for stratifying RA outcome, regardless of disease duration or effects of immunosuppressive therapy. Extraordinary elevation of sE-Selectin has been found to be associated with severe manifestations of RA. Unlike CRP, soluble intercellular adhesion molecule 1 [sICAM-1], RF, and ANA, sE-Selectin discriminates between mild and severe RA.
2. Anti-CCPs appear to have a high specificity [90-98 percent] in RA and thus may prove useful in early diagnosis, even though the sensitivity of the test is about 50-65 percent at presentation. Interestingly these antibodies may be in the serum years before the onset of clinical disease.

IMAGING:
1. Radiographs of hands and feet can be used to assess the presence and progression of cartilage loss and bone erosions. The Larsen or Sharp scoring methods are devised standards to quantify these measures. The erosion count correlates with physical function, and arrest or retardation of radiographic change is considered to be a marker of good control of disease.
2. MRI and CT are valuable in assessing neck pathology and pressure on cervical cord. MRI and high-frequency ultrasound examination are sensitive methods to evaluate synovitis and early change in cartilage and bone, but are as yet not in routine use [3].

3. DEXA scanning is in routine use for the assessment of bone mineral density [3].

MANAGEMENT OF RA:

The aims of treatment are: [3]

1. To relieve symptoms and signs of disease.
2. Maintain physical function.
3. Prevent structural damage to joints and associated physical structures.
4. Restore and maintain quality of life that permits the pursuit of normal work, domestic, and social life.
5. Reduce the comorbidity and increased mortality associated with the disease and therapies.
6. Correct abnormal laboratory-based values of haemotopoietic functions, acute phase proteins, and other markers of disease process.

Despite the best therapies in current use, the goal of halting structural damage and maintaining a normal quality of life have not yet been realized, although significant progress has been made. The realistic aims, therefore, are to maximize gains while minimizing toxicity of drugs [ an optimum risk : benefit ratio ] and operate within the pharmaco-economic constraints that apply in the patients treatment setting [3].

Generally, patients with severe and active disease will require more aggressive medical treatment than those with mild disease, the main aim being to control the disease as rapidly as possible with DMARDs started within three months of diagnosis. A useful intermediate goal, therefore, is to have all patients evaluated by a rheumatologist within three months after onset of symptoms [24].
With aggressive and continuing use of available therapeutic agents it is possible to achieve remission in 20 to 40% of patients over a period of 1 to 2 years, with the benefit likely to be most marked in early disease.

Remission is rare in established RA of more than 2 to 3 years duration. Nevertheless minimizing disease activity by attention to a measurable response to therapy remains at the core of the management plan. The provision of holistic care requires team work and co-ordination between the treating physician and other medical and health care professionals, including specialist nurses, physiotherapists, occupational therapists, social workers, and surgeons [3].

QUALITY OF LIFE ISSUES IN RA:
Quality of life issues are of great importance in RA since it is a disease that is progressively debilitating in many ways such as life long pain, progressively worsening physical disability and deformities. Patients with RA are condemned to a life of obligatory dependence on expensive drugs with harmful side effects for temporary relief of pain and to retard the progressive physical disability. Such patients who are still in employment are faced with the bleak prospect of loss of such employment and hence loss of income, social status, social support, independence, and social distraction [3]. Patients with RA also have a significantly higher level of comorbid conditions, especially infections and cardiovascular disease [3]. RA therefore affects negatively all aspects of quality of life such as physical functioning, social functioning, emotional functioning, mental health, and general health [26]. Functional capacity, as studies have shown, is strongly influenced by disease activity throughout the course of RA. Use of DMARDs together with NSAIDs therefore impact positively on quality of life in patients with RA [27].

Over the past 20 years various instruments called Health Related Quality Of Life [HRQOL] patient questionnaires, both generic and specific, have been developed and used for assessing the effects of RA on various aspects of the patients life [27, 30].
Such assessments are carried out as baseline, and subsequently at regular intervals, to monitor the effects of treatment on the activity of the disease, quality of life, and functional capacity.

Assessing patient-centered outcomes in RA has become a high priority for patients and providers, particularly in the light of newer and more effective treatment options aimed at maintaining good functional capacity. Currently there is no single clinical or laboratory variable that can completely measure disease activity or treatment response, but HRQOL questionnaires have been shown in studies to give a more accurate assessment of the patients disease, functional status, and well being [31, 32].

Newer HRQOL instruments continue to be developed, which are both multidimensional and disease-specific with additional discriminant validity, to meet the emerging realities of RA and its treatment in the 21st century [33]. The instruments selected for use in this study, however, are among the most widely used in rheumatology to date because of their reliability, validity, sensitivity, and responsiveness to change [30]. These are the SF-36 and DAS-28, each is discussed in more detail below.

DISEASE ACTIVITY MEASURES.

Disease activity has been shown to be the most critical determinant of functional capacity at any given time throughout the course of RA. It is therefore one of the most important determinants of QOL in RA, especially in early disease when structural damage is still minimal [27].

The instrument most widely used currently to measure disease activity is the Disease Activity Score [DAS]. It combines single measures into an overall continuous measure of RA activity using a single index score scale with a range of 0 to 9.4.

The use of a single index has advantages because simultaneous interpretation of several measures of RA activity is difficult. It also has advantages for statistical analysis in studies.
There are four subtypes of DAS, and the subtype used in this study is DAS-28 [30]. This instrument basically combines clinical indices of swollen and tender joints, out of a count of 28 joints, with the patient's ESR / CRP value and General Health assessment on a visual analogue scale to compute the DAS score.

QUALITY OF LIFE MEASURES.
For this study we will use SF-36, which is the most widely used generic [not disease specific] instrument worldwide, for measuring HRQOL. In its original version it contains the following dimensions: [30]

1. Physical functioning - which assesses disease impact on basic physical activities such as running, walking, climbing stairs, lifting, e.t.c.
2. Role limitations due to physical problems - reduced working time, reduced amount of work done, inability to do particular kinds of work, needing extra effort to do same amount of work, e.t.c.
3. Bodily pain - how much it interferes with work, both domestic and outside home.
4. Social functioning - whether able to participate in social activities [visit friends, attend parties, e.t.c].
5. Mental health - whether depressed or anxious.
6. Role limitations due to emotional problems.
7. Vitality and overall / general health.

See appendix 2 for a specimen of SF-36.

MEASURES OF ADULT GENERAL FUNCTIONAL STATUS.
There are at least five instruments currently in use in this category but the HAQ, a disease specific instrument, is the most widely used instrument in rheumatology for it's high reliability and validity. The original HAQ covers five dimensions of functional outcomes, but the version most commonly used includes only the disability index, the visual analogue pain scale, and the VAS patient global assessment [30].
VARIABILITY OF QOL IN RELATION TO TREATMENT IN RA.

There is documented evidence that functional capacity, and therefore QOL, in RA patients is influenced by multiple variables. The variables most frequently suggested are disease activity, joint destruction, and psycho-social characteristics of each individual patient [27].

Studies have further shown that whereas disease activity is a strong determinant of functional capacity throughout the course of RA, the contribution from joint destruction becomes increasingly important with time, and is the main determinant of functional capacity later in the disease course [27]. Achieving maximal control of both disease activity and joint destruction early in the disease by use of DMARDs is thus of great importance in improving QOL throughout the course of RA. Medications that are used to treat RA are divided into three main classes: NSAIDs, Glucocorticoids, and DMARDs – both synthetic and biologic.

NSAIDS.

These anti-inflammatory analgesics reduce pain, swelling, and stiffness of joints in active RA. This group of drugs is therefore capable of causing functional improvement, but without retarding the progression of disease [25]. In the long-term treatment of RA, therefore, these drugs must be used alongside DMARDs. NSAIDs are however particularly helpful alone during the first few weeks before a definitive diagnosis of RA can be established. NSAIDs, especially in long-term use, may also have negative impact on QOL by their side effects profile which may include gastrointestinal ulcerations, perforation, and hemorrhage, and NSAID induced nephropathy [25].

GLUCOCORTICOID.

Glucocorticoids are potent suppressors of the inflammatory response in RA. Low-dose oral glucocorticoids [<10mg of prednisone daily, or the equivalent] and local injections of glucocorticoids are highly effective in relieving symptoms in patients with active RA. A patient disabled by active polyarthritis may experience marked and rapid improvement in functional status within a matter of days following initiation of low-dose glucocorticoids.
Frequently, disabling synovitis recurs when glucocorticoids are discontinued, even in patients who are receiving combination therapy with one or more DMARDs. Therefore, many patients with RA are functionally dependent on glucocorticoids and continue them long-term [24]. Controversy continues about when, if, and how these compounds should be used to treat RA.

Studies conducted more recently have corroborated earlier findings that glucocorticoids decrease the progression of RA as detected radiologically. These drugs therefore confer a long-lasting improvement of QOL in patients with RA. This may however be countered by their predictable side effects even at minimal doses used over prolonged periods of time as currently practiced.

The most common side effects include thinning of skin, cataracts, osteoporosis, hypertension, hyperglycemia, and hyperlipidemia [25].

SYNTHETIC DMARDs.

Optimal management of RA requires early, rapid, and sustained suppression of inflammation and joint destruction with DMARDs, which are defined as medications that retard or halt progression of disease [25]. DMARDs are therefore the most effective drugs at bringing about a lasting improvement of QOL in patients with RA. A meta-analysis of blinded clinical trials has suggested that the efficacy of methotrexate [MTX], sulfasalazine [SSZ], intramuscular gold, and penicillamine is similar [25]. Anti-malarial drugs [chloroquine and hydroxychloroquine] are less effective. Penicillamine, because of its toxicity, and oral gold, because of its marginal efficacy, are rarely used today. Since observational trials have clearly identified MTX as the synthetic DMARD that is most likely to induce long-term response, with a long-term track record of acceptable toxicity and low cost, it is most often selected for initial therapy. MTX can be both hepatotoxic and teratogenic [25].
BIOLOGIC DMARDs.

Three biologic products that inhibit the actions of TNF-alpha [infliximab, etanercept, and adalimumab], and one that inhibits the action of IL-1 [anakinra], are now available to treat RA. There is also renewed interest in products that target the activation of T-cells or B-cells, including the anti-CD 20 [rituximab], in the treatment of RA [25]. It has been shown in clinical trials that patients with early RA and those with active RA inspite of DMARD therapy improved on etanercept. Infliximab is currently recommended for use only with concomitant MTX therapy.

Randomized controlled trials have shown that the biologic DMARDs, in combination with MTX, have a significant contribution to improvement of functional capacity and QOL beyond that achieved by MTX alone. In these trials of etanercept and infliximab many patients improved rapidly, even during the first two weeks of treatment [25, 24, 34].

COMBINATION THERAPY WITH DMARDs.

Conventional treatment with a single DMARD often fails to adequately control clinical symptoms or prevent disease progression. As a result, rheumatologists are increasingly prescribing combination DMARD therapy [29]. Randomized controlled trials have demonstrated that the triple DMARD combination of MTX, SSZ, and hydroxychloroquin [HCQ] has substantially increased efficacy compared to MTX alone, or to HCQ plus SSZ, without increased toxicity [36, 37].

Recently, the triple DMARD combination of MTX, SSZ, and HCQ has been shown to be superior to double DMARD combinations of MTX plus SSZ, or MTX plus HCQ, in both early [38] and more advanced [39] RA. Whether to start a course of low dose glucocorticoid initially along with a chosen DMARD is controversial; many clinicians start treatment with prednisone 5-7.5mg / day as a bridge therapy, until the slower acting DMARDs have a chance to work, then taper the glucocorticoid. Questions being asked include whether rapid disease suppression should be induced with steroids or TNF-alpha inhibitors which would then give way to the more affordable synthetic DMARDs [25].
STUDY JUSTIFICATION

1. Assessing patient-centered outcomes, such as QOL and severity of disease, in RA has become a high priority for patients and providers when trying to understand the influence of interventions on the disease, or the impact of the disease on patients and their families. The need to carry out a study such as this one in our local setting cannot therefore be over emphasized.

2. Currently it is of critical importance to start patients with rheumatoid arthritis on appropriate DMARD regimen early [within 3 months of diagnosis], yet there is a clinical impression that the treatment of rheumatoid arthritis in our local setup is rather haphazard. There is therefore a need to carry out a study such as this to establish the true situation as regards treatment of rheumatoid arthritis in our local setting.

3. This study is intended to provide results that may be useful, not only in improving the management and QOL of our RA patients, but also in serving as a basis for appropriate further research.
STUDY AIM AND OBJECTIVES:

AIM: To determine the socio-demographic, clinical, and QOL profiles in patients with RA at KNH.

OBJECTIVES:

1. To determine age, gender, level of education and employment status of patients with RA at KNH.
2. To determine clinical patterns of presentation, severity of disease scores, and QOL in patients with RA at KNH.
3. To determine modes of treatment employed, including which drugs [whether NSAIDs, DMARDs, or steroids], surgery, physiotherapy, psychiatric, or occupational therapy, in patients with RA at KNH.
4. To relate the patients’ QOL [SF-36 scores] to their ages, duration of illness, gender, level of education, employment status and types of drug treatment [DMARD, NSAID, + STEROIDS].
5. To relate the patients’ severity of disease [DAS-28 scores] to their ages, duration of illness, gender, level of education, employment status, and types of drug treatment [DMARD, NSAID, + STEROIDS].

STUDY DESIGN:

This was a cross-sectional descriptive study.

STUDY SITE:

The study was conducted in the medical outpatient clinic at the KNH.

METHODS AND PATIENTS.

Procedure: Memos to clinicians soliciting for patients were posted in casualty, orthopaedic wards and clinic, medical wards and outpatient clinic, physiotherapy and occupational therapy departments, departments of medicine and surgery, and in the records department at the KNH. Patients referred for the study with established or suspected diagnosis of RA were screened consecutively.
Operational [case] definition of RA: RA was defined as per the American College of Rheumatology 1987 revised criteria for the classification of RA-see appendix 1 for details.

Inclusion criteria: Those patients aged thirteen years and above who also met the ACR criteria for the diagnosis of rheumatoid arthritis.

Exclusion criteria:
- Patients who declined to sign consent.

CLINICAL METHODS

Patients meeting the inclusion criteria were enrolled into the study, were thereafter interviewed and examined physically with particular attention to the following:

1. Socio-demographic data, specifically relating to age, gender, level of education, and whether in paid employment or not.
2. The patient’s medical history relating to how and when RA was diagnosed, and treatment history for the past six months specifically relating to any use of NSAIDs, DMARDs, or steroids [intra-articular or systemic], surgery, physiotherapy, psychiatric and occupational therapies. Review of systems for any co-morbidity or extra-articular complications of RA.
3. General and systemic physical examination, taking note of any co-morbidity and any complications of RA.
4. To find out which particular joints are involved in the disease process.
5. To examine for the presence or otherwise of rheumatoid nodules.

This information was documented using questionnaires filled by the investigator.

QOL / DAS-28 CATEGORIES:

1. DAS-28 was categorized as: ≤ 2.6 [remission], > 2.6-3.2 [mild], > 3.2-5.1 [moderate], > 5.1 [high].
2. QOL scores were categorized as: 0-40 [poor], 41-60 [fair], 61-80 [good], 81-100 [very good].
LABORATORY METHODS:

Blood was collected by the investigator as per standard phlebotomy procedures, whereby 3mls of blood was drawn at once and put into two separate bottles as follows:

1. 2mls of blood was put into a bottle with EDTA used for full blood count [FBC] and ESR determination. Analysis was done using a CELDYN 3200 series coulter machine for FBC, and Wintrop method for ESR. Normal ESR by this method are 0-20mm/hr and 0-9mm/hr for females and males respectively.

2. 1ml of blood was put in a plain bottle for the determination of IgM rheumatoid factor using RA LATEX TEST, which is a standard latex agglutination test with both negative and positive controls. With this test the presence of agglutination indicates a level of RF in the sample equal to or > 8 I.U / ML, while a negative result indicates a level of RF in the sample of < 8 I.U / ML. Blood for RF test will only be drawn from those patients without a previous positive RF test result.

SAMPLING METHOD AND SAMPLE SIZE: Patients were seen consecutively and all consenting patients who met the inclusion criteria were included in this study. Sample size was duration limited and, since rheumatoid arthritis is not a very common disease, the study was conducted for seven months to achieve a reasonable number of patients.

DATA ANALYSIS:

1. Data collected was coded, transferred into the computer, cleaned, and organized to suit statistical analysis using SPSS computer software package.

2. Continuous variables were categorized in ranges and summarized into means, medians, modes, and standard deviations. Quantitative data was presented in frequency distribution tables and bar diagrams. Categorical data was presented in pie-charts.

3. Relationships between two continuous variables, for example QOL and age, QOL and duration of illness, QOL and DAS, were analyzed by Pearson correlation coefficients [if variables normally distributed] or by Spearman rank correlation [if variables not normally distributed].
4. Relationships between continuous variables and categorical data, for example QOL and gender, or QOL and employment status were analyzed by t-test method [if variables normally distributed] or by Mann-Whitney U test [if variables not normally distributed], while that between QOL or DAS and type of drug treatment or level of education were analyzed using one way ANOVA [if variables normally distributed] or Kruskal-Wallis one way ANOVA [if variables not normally distributed]. A significant association was deemed present at a p value of < 0.05.

STUDY LIMITATIONS:

1. The study was hospital based and is therefore likely to have been biased against otherwise qualified patients who were unable to afford hospital attendance and those who didn’t feel ill enough to seek treatment.
2. The study used case definition based only on ACR and therefore stands a chance of missing out on atypical presentation of RA.
3. It is a cross-sectional study and therefore more limited at determining effects of drug treatments or otherwise on disease outcome than would a longitudinal study.
4. Extra-articular manifestations of RA looked for only clinically, therefore there is a possibility that they were missed.

ETHICAL CONSIDERATIONS:

1. The study was done after receiving consent from the department of medicine [University of Nairobi] and the KNH ethical and research committee.
2. The study was only carried out on adult patients who had given informed consent, and on those below the age of 18 years only with informed consent of their parents or legally recognized guardians. See appendix 4 for a specimen of the consent form.
RESULTS

A total of 180 patients, aged thirteen years and above, were screened for rheumatoid arthritis from 6th of September 2005 up-to 4th of April 2006. Sixty of them satisfied the inclusion criteria and were recruited for the study. Of the 60 patients, 8 were male and 52 female [M: F = 1: 6.5].

Mean age of patients was 41.38 ± 16.78 [range was 14 to 85 years]. There were two peak age brackets, 20 – 29 and 40 – 49 years. The age distribution of the recruited patients is as shown in fig. 2.

Table 1: Characteristics of the study population.

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>POPULATION [N = 60]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: Female ratio</td>
<td>1: 6.5</td>
</tr>
<tr>
<td>Age: 14- 85 years</td>
<td>41.38 ± 16.78</td>
</tr>
<tr>
<td>Level of education [%]</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>11.7</td>
</tr>
<tr>
<td>Primary</td>
<td>40.0</td>
</tr>
<tr>
<td>Secondary</td>
<td>28.3</td>
</tr>
<tr>
<td>College</td>
<td>13.3</td>
</tr>
<tr>
<td>University</td>
<td>5.0</td>
</tr>
<tr>
<td>Disease duration [Months] 1-300.</td>
<td>64.97 ± 85.02 [Median= 24]</td>
</tr>
<tr>
<td>Joint involvement – MCPJ and PIPJ [%]</td>
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</tr>
<tr>
<td>Rheumatoid factor positive [%]</td>
<td>78.9</td>
</tr>
<tr>
<td>Rheumatoid nodules present [%]</td>
<td>13.3</td>
</tr>
<tr>
<td>DAS-28 [%]</td>
<td></td>
</tr>
<tr>
<td>Remission [≤ 2.6]</td>
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</tr>
<tr>
<td>Mild [&gt; 2.6-3.2]</td>
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</tr>
<tr>
<td>Moderate [&gt; 3.2-5.1]</td>
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</tr>
<tr>
<td>High [&gt; 5.1]</td>
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<tr>
<td>QOL categories [1-100] MC/PC [%]</td>
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<tr>
<td>Poor [0-40]</td>
<td>10/20</td>
</tr>
<tr>
<td>Fair [41-60]</td>
<td>25/38</td>
</tr>
<tr>
<td>Good [61-80]</td>
<td>30/22</td>
</tr>
<tr>
<td>Very good [81-100]</td>
<td>35/20</td>
</tr>
<tr>
<td>Drug treatment [%]</td>
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<tr>
<td>At least one DMARD</td>
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<td>Prednisone alone</td>
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<td>NSAID alone</td>
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<td>Co-morbid conditions [number]</td>
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<td>Hypertension</td>
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<tr>
<td>Peptic ulcer disease</td>
<td>5</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2</td>
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</tbody>
</table>

KEY: MC=Mental component, PC=Physical component, MCPJ=Metacarpo-phalangeal joint, PIPJ=Proximal Inter-phalangeal joint.
The percentage of the patients with level of education of primary school and below was 51.7%, while primary together with secondary level education accounted for the highest figure of 68.3%. The distribution of level of education among the study population is as shown in Table 2. A large majority of the patients [70.2%] were unemployed while the remaining 29.8% were in paid employment.

Table 2: The distribution of level of education among the study population.

<table>
<thead>
<tr>
<th>Level of education</th>
<th>Frequency</th>
<th>Percent</th>
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</thead>
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<td>7</td>
<td>11.7</td>
</tr>
<tr>
<td>primary</td>
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<tr>
<td>secondary</td>
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<td>28.3</td>
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<tr>
<td>college</td>
<td>8</td>
<td>13.3</td>
</tr>
<tr>
<td>university</td>
<td>3</td>
<td>5.0</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>98.3</td>
</tr>
<tr>
<td>Missing System</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100.0</td>
</tr>
</tbody>
</table>
The mean duration, in months, of rheumatoid arthritis was 64.97 ± 85.02 with both mode and median duration of 24 months [range was 1 to 300 months]. The distribution of disease duration among the study patients is as shown in Fig. 3.

**Fig. 3: The distribution of disease duration among the study patients**

![Bar chart showing disease duration distribution](image)

In 75% of the study patients, one or more of the metacarpophalangeal and proximal interphalangeal joints of the hand were involved by RA. Other frequently involved sites include wrists, elbows, knees, ankles and gleno-humeral joints of the shoulders. Four patients, three female and one male, had severe deforming and disabling joint disease.

Serum rheumatoid factor was positive in 78.9%, while rheumatoid nodules were present in 13.3%. Patients with rheumatoid nodules had moderate to severe disease.

A large majority of patients [88%] had active disease, with mild disease accounting for 18%, moderate disease 38% and severe disease 32%. The remaining 12% of the patients had inactive disease [remission]. The disease severity [DAS-28] pattern is illustrated in Fig. 4.
Fig. 4: Severity of disease [DAS-28] pattern in the study patients.

KEY: DAS-28 was categorized as: ≤ 2.6 [remission], > 2.6-3.2 [mild], > 3.2-5.1 [moderate], > 5.1 [high].

There was no correlation between disease activity score and duration of illness \([p = 0.38]\), age \([p = 0.69]\), level of education \([p = 0.92]\) and employment status \([p = 0.52]\) among the study patients.

Fifty-eight percent of study patients had physical component QOL scores ranging from poor to fair compared to sixty-five percent who had mental component QOL scores ranging from good to very good. The percentage distributions of physical and mental component QOL summary scores for the study patients are as illustrated in fig. 5.
KEY: QOL scores were categorized as: 0-40 [poor], 41-60 [fair], 61-80 [good], 81-100 [very good].

There was no significant association between QOL summary scores and level of education [p values of 0.79 and 0.30 for physical and mental components respectively], employment status [p = 0.73 and p = 1 for physical and mental components respectively], duration of illness [p = 0.155 and p = 0.435 for physical and mental components respectively] and patient’s age [p = 0.617 and p = 0.193 for physical and mental components respectively] in the study subjects. Both physical and mental health QOL summary scores however showed significant negative correlations with disease activity scores [Pearson correlation coefficients of – 0.603 and – 0.632 respectively, p< 0.001 for both] among the study patients.

Twenty-eight [46.7%] of the sixty study patients were on treatment with at least one disease modifying anti-rheumatic drug [DMARD] from a selection of methotrexate [MTX], sulfasalazine [SSZ], hydroxychloroquin [HCQ] and the biologic leflunomide [Arava]. The most commonly prescribed DMARD was MTX in 26 [43.3%] of the sixty study patients, followed by SSZ in nine
patients [15%] and HCQ in three patients [5%]. There were two patients on the triple DMARD combination therapy of MTX, SSZ and HCQ. The most frequent drug combination was MTX plus prednisone in 18 [30%]. Forty [66.7%] of the sixty study patients were on oral prednisone with only five [12.5%] taking oral calcium supplements.

Fifteen patients [25%] took only non-steroidal anti-inflammatory drugs while Eighteen [30%] of the study patients took drugs only intermittently. Three of the sixty study patients could not recall the drugs they had used, while one patient had not been on any drug therapy despite severe disease [DAS-28 of 6.12]. Of the patients on prednisone 25 [62.5%] were taking high dose [10 mg or more] while 15 [37.5%] were on low dose [< 10 mg]. The distribution of drug treatment in the study population is summarized in table 3. Four of the study patients with severe disease not responding to the synthetic DMARDs, were on leflunomide.

**Table 3: Distribution of drug treatment among the study patients**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Frequency</th>
<th>% of study patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX + Prednisone</td>
<td>18</td>
<td>30.00</td>
</tr>
<tr>
<td>MTX + SSZ + Prednisone</td>
<td>5</td>
<td>8.00</td>
</tr>
<tr>
<td>MTX + HCQ + Prednisone</td>
<td>1</td>
<td>1.67</td>
</tr>
<tr>
<td>SSZ + Prednisone</td>
<td>2</td>
<td>3.33</td>
</tr>
<tr>
<td>MTX + SSZ + HCQ + Prednisone</td>
<td>2</td>
<td>3.33</td>
</tr>
<tr>
<td>NSAIDs Alone</td>
<td>15</td>
<td>25.00</td>
</tr>
<tr>
<td>Prednisone Alone</td>
<td>13</td>
<td>21.70</td>
</tr>
<tr>
<td>No drug</td>
<td>1</td>
<td>1.67</td>
</tr>
<tr>
<td>No recall</td>
<td>3</td>
<td>5.00</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100</td>
</tr>
</tbody>
</table>
One patient, a female, out of the sixty study patients had undergone corrective surgery for complications of rheumatoid arthritis. She had bilateral hip joint replacement and corrective surgery for a badly damaged left knee joint. Thirteen of the study patients had been on physiotherapy; three on occupational therapy and one had psychiatric management.

Twenty out of the sixty study patients had at least one co-morbid condition as presented in table 4. The most common co-morbid condition was arterial hypertension, accounting for 11 out the 20, followed by peptic ulcer disease [5 patients] and diabetes mellitus [2 patients].

**Table 4: Co-morbid conditions among the study patients.**

<table>
<thead>
<tr>
<th>Co-morbid conditions</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN</td>
<td>6</td>
<td>10.0</td>
</tr>
<tr>
<td>PUD</td>
<td>3</td>
<td>5.0</td>
</tr>
<tr>
<td>eye</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>cataract</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>PTB</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>skin lesions</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>HHD</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>fibroids</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>asthma</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>HTN &amp; PUD</td>
<td>2</td>
<td>3.3</td>
</tr>
<tr>
<td>HTN &amp; DM</td>
<td>2</td>
<td>3.3</td>
</tr>
<tr>
<td>Anaemia</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>33.4</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100.0</td>
</tr>
</tbody>
</table>
DISCUSSION

The sixty patients with rheumatoid arthritis seen in this study in a period covering only seven months shows that the number of cases seen at KNH with this diagnosis have risen markedly over the years. This is so because in the last documented study on RA at KNH by Bagg et al and published in 1979 [15], they managed to see 76 patients with RA over a much longer period of eighteen months. This rise in the number of cases may be a reflection of increasing health awareness among Kenyans, a better referral system, the presence of a rheumatology clinic at KNH, or it could be as a result of increasing urbanization in Kenya, as studies in South Africa and in the USA have shown increased prevalence of RA in urban compared to rural populations [3]. It could also be as a result of the difference in the population of Nairobi between then and now. On the other hand there could be a true rise in the prevalence of RA in Nairobi, but that can only be ascertained by conducting a well-designed community based study.

The mean age of patients of 41.3 recorded in this study is lower than the 43 years by Bagg et al [15], and the 44.5 years by Oyoo [49], although the double peak age groups of 20-29 years and 40-49 years recorded in this study did not feature in their studies. The age characteristics found in the three studies are however younger compared to those recorded in a study in the United Kingdom by Wiles et al [41], who found a peak age of 45-74 years for females and 65-74 years for males. This difference could probably be a reflection of the generally younger Kenyan population compared to that of the United Kingdom. Similarly younger age groups in black patients [36.6 years] compared to caucacian patients [44.2 years] with RA have however been recorded in South Africa by Mody [42], and by Adebajo and Reid in a study in Nigeria [43], and could therefore probably be due to a real racial difference.

The median duration of illness of 24 months is much lower compared to the 48 months recorded by Bagg et al [15], probably reflecting increased health awareness and improved accessibility of health services over the years, probably coupled with early referral for specialized care.
The male to female ratio of 1:6.5 recorded in this study is close to the 1:5 by Oyoo [49], but markedly higher than the 1:2.8 by Bagg et al [15], the 1:1.5 in Nigeria by Adebajo and Reid [43], the 1:1.7 in Uganda by Kanyerezi and Lutalo [13], the 1:2.3 in Zimbabwe by Lutalo [44] and the 1:3.7 found in Durban, South Africa by Mody and Meyers [45], all of which are comparable with the 1:3 found in most caucasian studies [4]. The female preponderance widely reported in RA is thus accompanied by wide regional variation and indeed, in a study in Nigeria, no significant difference between the number of males and females with RA was recorded [50]. A community based study is however necessary in order to come up with a more reliable figure for the local population.

Slightly more than half (51.7%) of the study patients had a level of education of primary school and below, while the majority (70.2%) were not in paid employment. This could probably reflect an institutional bias, most probably linked to the fact that KNH is a public institution likely to be attended by patients of low socio-economic status, or it could be a reflection of the level of unemployment and education among the general Kenyan population. It is also possible that RA is commoner in the lower social classes of our society, but this needs to be investigated in a community-based study. The association of RA with low level of education and unemployment as shown in this study would imply that these patients are unlikely to afford unsubsidized health care.

In 75% of the study patients, one or more of the metacarpophalangeal and proximal interphalangeal joints of the hand were involved by RA. Other frequently involved sites include wrists, elbows, knees, ankles and gleno-humeral joints of the shoulders. Serum rheumatoid factor was positive in 78.9% of the study patients. The pattern of joint involvement with RA and the prevalence of rheumatoid factor positivity recorded in this study are similar to those recorded in earlier studies in Kenya by Bagg et al (15), Houba et al (20) and to that found in the Caucasians (3).
The presence of *rheumatoid* nodules was however recorded in 13.3% of patients in this study compared to 31.6% by Bagg *et al* (15), 25% in Cape Town, South Africa by Mody and Meyers (45), 7.9% and 12% in two Ugandan studies by Kanyerezi *et al* (12) and Lutalo (13), and in only 1.4% in Nigeria by Green Wood (9). The presence of rheumatoid nodules, normally a marker of severe disease, did not appear to predict accurately for severe disease in this study.

Apart from rheumatoid nodules there were however no other extra-articular manifestations of rheumatoid arthritis recorded in this study. The other African studies where severe extra-articular manifestations of RA has been noted to be a rare feature include those by Greenwood in Nigeria (9), Anderson in South Africa (46), Bagg *et al* (15). Exceptions have however been reported in black Africans in Uganda by Kanyerezi and Lutalo (13), Moolenburgh *et al* in Lesotho (47), and Mody and Meyers (45). In these studies a wide spectrum of extra-articular manifestations with involvement of the eye, lungs, heart, central nervous system, leg ulcers, hepatosplenomegally and lymphadenopathy were reported.

A large majority of patients [88%] had active disease, with mild disease accounting for 18%, moderate disease 38% and severe disease 32%. Only 12% of the study patients were in disease remission. Bagg *et al* (15) used a radiological criteria (X-ray changes graded according to criteria of Kellgren) to categorize disease severity as grades 0-1, 2, 3, and 4 in an ascending order of disease severity. Majority of their patients fell in grade 2 [38%] and 3 [36%], with 19% in grade 0-1 and only 7% in grade 4. Their findings, though not amenable to direct comparison with this study due to difference in criteria used, would seem to suggest that the disease in those patients was less severe than that recorded in this study. Yet, even then, their findings as to disease severity were comparable to those found in an English study by Thould *et al*, except for grade 4 disease which accounted for 15% in the English study (17).
Other studies in black populations have found markedly mild disease compared to that in Caucasians, for example in a study in Nigeria Greenwood found 69% in Kellgren grade 0-1, 21% in grade 2, 8% in grade 3 and only 2% in grade 4 (9,15). Adebajo and Reid did a comparative study between patients presenting with RA at a rheumatology unit in Nigeria and patients presenting to a British rheumatology unit. Apart from the West African patients being younger at disease onset with less frequent family history, fewer extra-articular features, fewer erosions and less commonly rheumatoid factor positive, the overall mildness of their disease was striking (43). In another comparative study between pure black Bantu Zimbabwean and British white patients with RA, Chikanza et al found that the Zimbabwean patients had a disease that was clinically and radiologically less severe with fewer extra-articular features compared to British white patients (18). It would therefore appear that, even among the black Africans, there is a wide regional variation in the severity of rheumatoid arthritis.

The patients' level of education and employment status showed no significant associations with disease severity, even though social deprivation is now recognized to have an important negative impact on morbidity and mortality in patients with RA independent of compliance with treatment and disease duration (28). The lack of association recorded in this study could be due to small study sample, or presence of confounders like not receiving proper drug treatment, or both. There was no significant association between severity of disease and age among the study patients. It has been suggested that advanced age at onset of RA is associated with severe disease, but not in an independent manner since aggressive disease is largely restricted to those elderly patients with high titers of rheumatoid factor (48). The lack of association recorded in this study is therefore not unique. Similarly the lack of significant association between duration of illness and severity of disease was not an unexpected finding. It would however require well-designed longitudinal studies to investigate these associations.
Fifty-eight percent of study patients had physical component QOL scores ranging from poor to fair, compared to sixty-five percent who had mental component QOL scores ranging from good to very good. Both component scores showed no significant association with age, level of education, employment status, or duration of illness among the study patients. One would have expected unemployment and low level of education, as markers of low socio-economic status, to be associated negatively with the QOL summary scores among the study patients. Similarly the lack of association between QOL and duration of illness is unexpected since functional capacity, and therefore QOL, is expected to deteriorate with time (27). The lack of association could probably be due to strong adherence to effective coping mechanism together with strong family / social support among the study patients.

Both physical and mental health QOL summary scores however showed significant negative correlations with disease activity scores [Pearson correlation coefficients of –0.603 and –0.632 respectively, p< 0.001 for both] among the study patients. This is an expected association since disease activity is the critical determinant of functional capacity throughout the course of rheumatoid arthritis (27). The predominantly moderate to severe disease activity and its significant negative correlation with the QOL summary scores therefore tends to point towards poor QOL among our study population.

Forty-six percent of the study patients were on treatment with at least one DMARD, the most commonly prescribed being MTX in 43% of the total study population. SSZ and HCQ were used by 15% and 5% of the study population respectively. There were only two patients on the triple DMARD combination of MTX, SSZ and HCQ in a study population with 70% moderate to high disease activity. However these were mostly recent referrals who had not been under the care of a rheumatologist for any reasonable period of time.
The scenario is quite different in the developed world where, with adequate drug therapy under the care of rheumatologists, they have been able to achieve disease remission in up-to 95% of their patients (51) compared to the 12% remission recorded in this study. The possible contributing factors to the low remission rate recorded in this study include poor compliance with medication, financial constraints and poor management due to scarcity of adequately trained medical personnel.

66.7% of the study patients were on oral prednisone with 62% of them taking high dose [10mg or more of prednisone / day], while only 12% of all those on prednisone took calcium supplements. This is in contrast to the current established practice of using low dose prednisone [<10mg / d], in combination with calcium supplements, as a bridge to effective DMARD therapy to guard against the common side effects of steroids such as thinning of skin, hypertension, impaired glucose tolerance, dyslipidemia and osteoporosis. Low dose prednisone has been shown to be as effective as high dose prednisone, but with an added advantage of less drug side effects (25). Similarly twenty-five percent of the study patients were on NSAIDs alone, despite the fact that NSAIDs alone have no place in the current management of rheumatoid arthritis as they have not been shown to slow down the progression of disease (25).

One patient, a female, out of the sixty study patients [1.67%] had undergone corrective surgery for complications of rheumatoid arthritis. She had bilateral hip joint replacement and corrective surgery for a badly damaged left knee joint. Thirteen [21.67%] of the study patients had been on physiotherapy; three [5%] on occupational therapy and one [1.67%] had psychiatric management. The percentage of patients needing surgery seems rather low in the background of a prevalence of active disease of 88%. Probably the very disabled did not seek treatment at KNH, or most of them were seen only by orthopaedic surgeons. The low percentage of patients receiving psychiatric management probably reflects adoption of other effective mechanisms such as optimism, comforting cognition, and social / family support to cope with the pain, disability and dependence attendant on RA.
A total of twenty out of the sixty study patients [33.4%] had various co-morbid conditions as presented in table 8. The most common co-morbid condition was arterial hypertension accounting for 11 out of the 20, followed by peptic ulcer disease [5 patients] and diabetes mellitus [2 patients]. Some of these co-morbid conditions probably arose as side effects of prednisone and NSAID therapy but it is not possible to establish causation from this study.

**CONCLUSIONS:**

From the results of this study rheumatoid arthritis affected a younger population of patients, with a female to male ratio that was two times that observed in the west. It affected mainly the unemployed with low level of education. The most common pattern of joint involvement was that of hands, wrists, elbows, shoulders, knees and ankles. A large majority of the patients had active disease, mostly moderate to severe, with only a small minority in disease remission. Less than half of the patients were on DMARDs, while a significant number of patients were on NSAIDs alone. Majority of the patients were on treatment with prednisone, mainly high dose. Physical component QOL scores ranged from poor to fair as compared to the mental component QOL scores which ranged from good to very good in the majority of patients.

**RECOMMENDATIONS:**

There is an urgent need to implement appropriate treatment guidelines in order to get majority of our patients into early disease remission. This will, no doubt, call for availability of well trained personnel in the field of rheumatology. There is need to conduct a comparative QOL study using the same SF-36 version on patients with a different disease entity. There is a need to conduct a study on the effects of co-morbidity on QOL of patients with RA.
REFERENCES:


# ACR CRITERIA FOR THE CLASSIFICATION OF RA

**CRITERION** | **DEFINITION**
--- | ---
1. Morning stiffness | Morning stiffness in and around joints, lasting at least one hour before maximal improvement.
2. Arthritis of three or more joint areas | At least three joint areas simultaneously have had soft tissue swelling or fluid [not bony overgrowth alone] observed by a physician. The fourteen possible areas are right or left PIP, MCP, wrist, elbow, knee, ankle, and MTP joints.
3. Arthritis of hand joints | At least one area swollen [as defined above] in a wrist, MCP, or PIP joint.
4. Symmetric arthritis | Simultaneous involvement of the same joint areas [as defined in 2] on both sides of the body [bilateral involvement of PIPs, MCPs, or MTPs is acceptable without absolute symmetry]
5. Rheumatoid nodules | Subcutaneous nodules, over bony prominences, or extensor surfaces, or in juxta-articular regions, observed by a physician.
6. Serum rheumatoid factor | Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in < 5% of normal control subjects.
7. Radiographic changes | Radiographic changes typical of RA on postero-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].

For classification purposes, a patient shall be said to have rheumatoid arthritis if he / she has satisfied at least four of these seven criteria. Criteria 1 through 4 must have been present for at least six weeks. Patients with two clinical diagnoses are not excluded. Designation as classic, definite, or probable rheumatoid arthritis is not to be made [2].
APPENDIX II

Name ___________________________________________ date __________________________

Those questions concern your health now and in the past. Please answer every question. If you are unsure of how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

2. Compared to 6 months ago, how would you rate your health in general now?
   1. Much better now than 6 months ago  2. Somewhat better now than 6 months ago
   3. About the same as 6 months ago  4. Somewhat worse now than 6 months ago
   5. Much worse now than 6 months ago

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

<table>
<thead>
<tr>
<th>Activity</th>
<th>Yes, Limited A Lot</th>
<th>Yes, Limited A Little</th>
<th>No, Not Limited At All</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Vigorous activities, such as running, lifting heavy objects,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>participating in strenuous sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Moderate activities, such as moving a table, pushing a vacuum cleaner,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bowing, or playing golf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Lifting or carrying groceries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Climbing several flights of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Climbing one flight of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Bending, kneeling, or stooping</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Walking more than a mile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h. Walking several blocks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. Walking one block</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>j. Bathing or dressing yourself</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Problem</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Cut down the amount of time you spent on work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Accomplished less than you would like</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Were limited in the kind of work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Had difficulty performing the work or other activities (for example,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>it took extra effort)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?
   a. Cut down the amount of time you spent on work or other activities
   b. Accomplished less than you would like
   c. Didn’t do work or other activities as carefully as usual

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

7. How much bodily pain have you had during the past 4 weeks?

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

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

   a. Did you feel full of pep?
   b. Have you been a very nervous person?
   c. Have you felt so down in the dumps that nothing could cheer you up?
   d. Have you felt calm and peaceful?
   e. Did you have a lot of energy?
   f. Have you felt worn out?
   g. Have you been a happy person?
   h. Did you feel tired?

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (such as visiting with friends, relatives, etc.)?
    1. All of the time  2. Most of the time  3. Some of the time  4. A little of the time  5. None of the time
11. How TRUE or FALSE as each of the following statements for you?

<table>
<thead>
<tr>
<th>Statement</th>
<th>Definitely True</th>
<th>Mostly True</th>
<th>Not Sure</th>
<th>Mostly False</th>
<th>Definitely False</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. I seem to get sick a little easier than other people</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. I am as healthy as anybody I know</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. I expect my health to get worse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. My health is excellent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Please check (✓) if this questionnaire is completed entirely by patient □ or with help □ from ____________________________

THANK YOU FOR COMPLETING THE QUESTIONNAIRE
APPENDIX III.

PATIENT QUESTIONNAIRE

DATE: ______________

NAME [initials only]: ___________________________ PATIENT NO. ______________

AGE [years]: _______________ PAID EMPLOYMENT: Yes No

SEX: M ___ F _____ LEVEL OF EDUCATION: Primary ___ Secondary ___
     College ___ University ___

DISEASE PROFILE

1. Disease duration since diagnosis: ______________

2. Symptoms, signs, and investigation results prior to diagnosis:

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Yes</th>
<th>No</th>
<th>Duration</th>
<th>Joints affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning stiffness of joints &gt; 1hr</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 hand joints</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 positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

   Full blood count result: Hb _________ gm/dl, WBCC___________ Platelets ___________
3. Treatment received since diagnosis:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Regular [yes/no]</th>
<th>Intermittent</th>
<th>Symptomatic</th>
<th>No recall</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Glucocort-HD [&gt;10mg/d]</td>
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<td>Glucocort-LD [&lt;10mg/d]</td>
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<td>Glucocort-IAI</td>
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<td>DMARDs: HCQ</td>
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<td>SSZ</td>
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<td>Biologics</td>
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<td>Other drugs:</td>
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Treatment received since diagnosis [continued]:

- Physiotherapy: Yes □ No □ Regular □ Intermittent □
- Occupational therapy: Yes □ No □ Regular □ Intermittent □
- Surgery: Yes □ No □ If yes, specify ________________________
- Psychiatric treatment: Yes □ No □

4. Are you currently on treatment for any other illness? Yes □ No □
   If yes, specify illness ________________________ drugs ________________________

5. Any co-morbid conditions or complications of RA on physical examination:
   Yes □ No □ Specify ________________________

6. DAS-28 examination:
   VAS = Visual Analogue Score for patient’s general health or global assessment of function:
   Question to patient: considering all the ways that your illness affects you, rate how you are doing on the following scale [show patient the sliding VAS scale ruler and record the number the patient indicates].

   Record sw28, which is the number of swollen joints from 28 joints, ______________

   Record TEN28, which is the number of painful joints from 28 joints, ______________

   Record the patient’s ESR in mm/hr, ______________
APPENDIX IV.

EXPLANATION AND CONSENT FORM

I am Dr. Bernard Owino, a post-graduate student in internal medicine at the University of Nairobi. I am carrying out a study on patients with rheumatoid arthritis to see how serious their disease is, which particular joints are affected, how this disease affects their lives as a whole, and what kind of treatments they are getting. The study forms part of the requirements for me to be able to obtain my Master of Medicine degree, but the results of the study are also intended to lead to recommendations which, if implemented, would lead to improved management and quality of life of patients with rheumatoid arthritis.

The study involves answering questions of personal nature as laid out in the two forms [SF-36 and the patient questionnaire], physical examination, and drawing of 3mls of blood. All the information you give and the examination and investigation results in this study will be handled with absolute confidentiality, and will not be divulged to any other person without your authority. You / he / she will feel a little pain, only as is normal with standard phlebotomy, when the blood is drawn, and the amount of blood drawn will not negatively affect your / his / her health.

Your / his / her participation in this study is absolutely voluntary and you / he / she will not be denied treatment or be in any way penalized for declining to participate.

Your / his / her participation in the study bears no extra cost to you / him / her, but the lab results will be used for your / his / her individual management.

I ___________________________ of ___________________________
Hereby consent / decline to participate in this study, the nature and purpose of which have been fully and satisfactorily explained to me.

Signed ______________________ [patient / parent / guardian] Date ________________

Witness signature ____________________________ Date ________________

INVESTIGATOR:

I ___________________________ hereby confirm that I am the investigator in this study, the nature and purpose of which I have fully explained to the patient / parent / guardian.

My contacts are: Dr. Benard Ouma Owino,
P.O. Box [00202] 19985, Nairobi,
Tel: 0722866668.

Investigator’s signature ________________ Date ________________