Research article

Chronic kidney disease in rheumatoid arthritis at Kenyatta National Hospital

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Abstract

Objective: To determine the prevalence of chronic kidney disease among patients with rheumatoid arthritis on follow up at the rheumatology outpatient clinic at Kenyatta National Hospital.
Design: Descriptive, cross-sectional study.
Setting: Rheumatology outpatient clinic at the Kenyatta National Hospital, a public national and referral hospital.
Subjects: Patients diagnosed to have rheumatoid arthritis who met the 2010 ACR-EULAR criteria.
Results: Out of 104 patients recruited, 93 (89.4%) were female with a female to male ratio of 8.5:1. Mean age of patients was 48.7(±15.6) years. Majority of the patients (90%) were on at least one Disease Modifying Anti-Rheumatic Drug (DMARD) with methotrexate being the commonest used. Other DMARDs were leflunomide, sulfasalazine and hydroxychloroquine. None of our patients was on a biologic agent. Use of NSAIDs and/or prednisone was very frequent (88.5%). Median duration of disease since time of diagnosis was 4 years. Majority of patients (60%) had active disease. We found the prevalence of chronic kidney disease to be 28.7% (95% CI 19.1-37.2%) based on estimated glomerular filtration rate using the Cockroft-Gault formula. Majority (50%) of which was stage 3a disease and none with end stage renal disease. We found no patients with proteinuria using urinary dipstick.
Conclusion: Although we did not find any proteinuria in our study population, prevalence of chronic kidney disease based on estimated glomerular filtration rate was high with the majority having early stages of kidney disease. Use of urine strips alone is not an adequate screening tool.

Introduction

Rheumatoid Arthritis (RA) is a worldwide health problem with an estimated global prevalence of 0.24%[1]. The World Health Organisation (WHO) considers it as one of the diseases with the greatest impact on society[2] and it is the 42nd highest contributor to global disability[1].

Patients with RA are at increased risk of death more than their age and sex matched non-rheumatoid controls. Even with improvement of disease management, there has been no decrease in mortality for patients with RA[3]. Renal disease is a common cause of mortality in patients with rheumatoid arthritis. This may be as a result of disease itself, drugs used in treatment and other causes of nephropathy[4]. As most patients with rheumatoid arthritis are above the age of forty years[5], age itself and other co-morbid conditions like diabetes and hypertension also have a negative impact on their kidney function.

Cardiovascular complications are the major causes of mortality in these patients. They are at higher risk of silent myocardial infarction and lower risk of angina pectoris. Mortality after these events is also higher than in their non-RA counterparts[6].

The effects of kidney dysfunction in RA are adverse. A low estimated Glomerular Filtration Rate (eGFR) increases Cardio-Vascular Disease (CVD) risk and vice versa. Since CVD is the major cause of mortality in these patients, frequent screening and modification of risk factors is of importance in this population[7].

Assessment of eGFR is also warranted in RA for drug adjustment. Methotrexate is the commonest Disease Modifying Anti Rheumatic Drug (DMARDs) used in the control of RA. Its use is contraindicated in any person with CKD stage 3 and above[8]. The use of other drugs, such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) must also be approached with caution in such patients as they can exacerbate kidney injury. CKD is progressive with rapid decline in function if it goes unrecognized and is not addressed early especially in the presence

of continued injury. Therefore screening for CKD is of vital importance especially in this group of patients who have several factors that may cause or worsen kidney damage.

Materials and Methods

Study population: The study was conducted on patients on follow up at the rheumatology outpatient clinic at the Kenyatta National Hospital which is the national referral hospital situated in Nairobi, Kenya. It is the sole clinic catering to patients with rheumatological illnesses in the public sector.

Patient recruitment: We screened patients with a file diagnosis of RA at the rheumatology outpatients' clinic consecutively until a sample size of 104 was reached. All patients aged 18 years and above who met the 2010 American College of Rheumatology –European League Against Rheumatism (ACR-EULAR) criteria[9] for RA and gave written informed consent were recruited. We recorded patients' age, gender, marital status, highest level of education acquired, disease duration and drug history on a data abstraction tool that had been prepared.

Patients underwent an assessment of disease activity using Disease Activity Score 28 (DAS 28)[10] which categorised them into remission, mild, moderate or severe disease. A blood pressure reading was taken using a mercury sphygmanometer. They were also weighed to the nearest kilogram. We requested patients to provide a urine sample for screening on site for a urinary tract infection and proteinuria using dipsticks.

Laboratory methods: An automated machine (Mindray BS 400) was used to determine creatinine levels which were subsequently used to calculate eGFR. The Wintrobe method was used to calculate ESR level for calculation of the DAS-28 score. We used the URIT 10V dipsticks to assess for proteinuria and urinary tract infection.

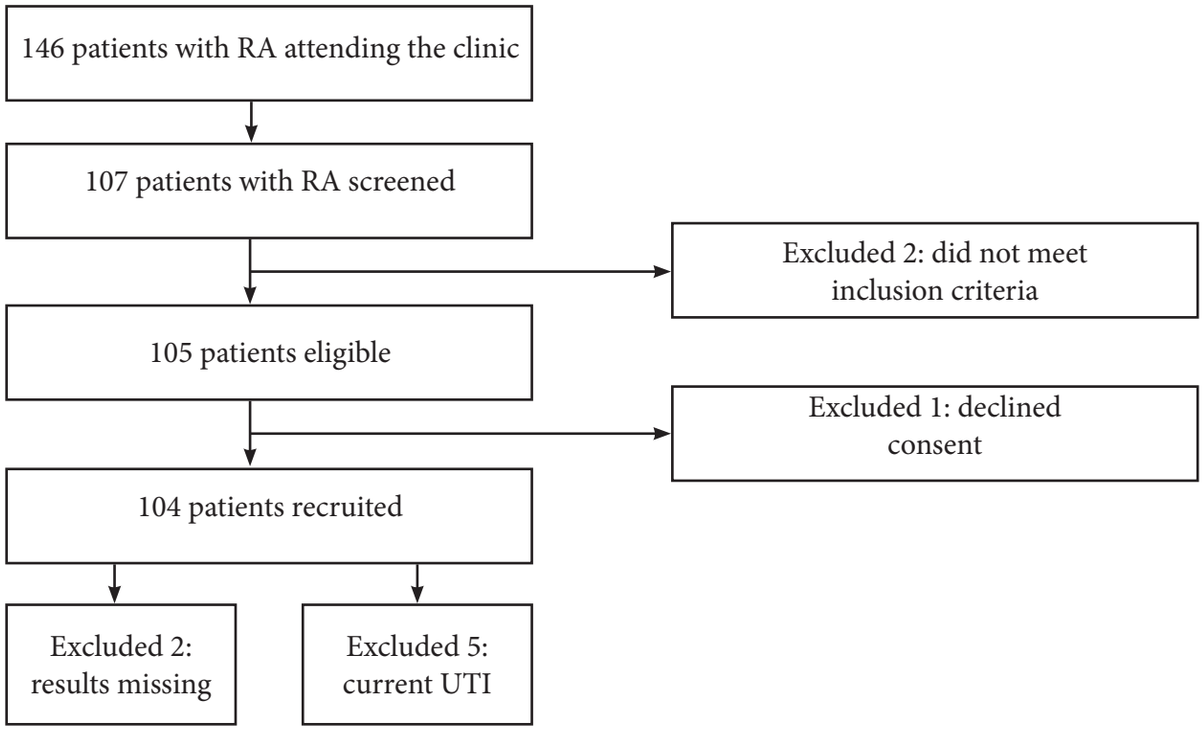
Ethical considerations: The study was undertaken after acquiring approval from the KNH Ethical and Research Committee. Only adults who were 18 years and above who gave written, informed consent were recruited.

Data analysis: Data was analysed using SPSS version 20 for Microsoft. Continuous variables were summarized into means, medians and standard deviations. Quantitative data was presented using frequency, tables, pie charts and bar graphs. Dependent variables were analysed for correlation with a p value of 0.05 or less considered significant. Chronic kidney disease was correlated with: disease duration using the Kruskal Wallis test, disease activity using the Spearman's correlation and treatment modality using the Chi-square test.

Results

Data was collected over a ten week period. Out of the population of 146 RA patients at the clinic we managed to screen a total of 107. Of these, two did not meet the inclusion criteria; one declined consent and was thus excluded, leaving a total of 104 patients who were enrolled. On screening for proteinuria, 5 patients were found to have a current UTI and were not evaluated for proteinuria. We evaluated 99 of the study participants for proteinuria. Of the total 104 patients screened, results for creatinine level were available for only 102. Figure 1 depicts patient recruitment.

Figure 1: Patient recruitment



In our study population, mean age was 48.7 ±15.6 years and majority of patients were female 93 (89.4%), married 71 (68.3%) and having attained some level of formal education 94 (90.4%). Table 1 shows their demographic and clinical characteristics. Comorbid diseases assessed were diabetes 8 (7.7%) and hypertension 37 (35.6%).

Table 1: Demographic and clinical characteristics of the study population (n=104)

Demographics	Frequency (n)	(%)
Age (years)		
18-24	7	6.7
25-34	11	10.6
35-44	26	25
45-54	24	23.1
55-65	20	19.2
65 and above	16	15.4
Sex		
Male	11	10.6
Female	93	89.4
Level of formal education		
None	10	9.6
Primary	41	39.4
Secondary	26	25
Tertiary	27	26
Marital status		
Married	71	68.3
Single	17	16.3
Divorced/separated/widowed	16	15.4
Disease duration since diagnosis (years)		
Less than 1	18	17.3
1-5	51	49
More than 5	35	33.7
Disease activity		
Remission	21	20.4
Mild	21	20.4
Moderate	39	37.9
Severe	22	21.3
Use of NSAIDs and prednisone		
NSAID + prednisone	43	41.3
NSAID	23	22.1
Prednisone	26	25
Not on NSAIDs or prednisone	12	11.5
DMARD use		
Yes	90	86.5

NSAIDs=Non-Steroidal Anti-Inflammatory Drugs, DMARD=Disease Modifying Anti-Rheumatic Agent

Prevalence of CKD: Of 104 patients, creatinine results were available for 102. Using the Cockroft-Gault formula, a total of 28 (27.5%) patients were found to have kidney disease. The staging for kidney disease was as follows; stages 3a (13.7%), 3b (7.8%) and stage 4 at (5.9%). There was no patient with stage 5 kidney disease. Table 3 gives the distribution of patients with CKD according to the KDIGO criteria.

Table 2: Stages of CKD

	Frequency (n)	(%)
CKD staging		
Stage 3a	14	50
Stage 3b	8	28.6
Stage 4	6	21.4

CKD= Chronic Kidney Disease

*Prevalence of proteinuria: T*he prevalence of proteinuria was found to be 0% among the 99 patients assessed.
Association of eGFR with duration of RA: eGFR was categorized into stages and an association with duration of disease analysed. There was no association found between the two variables (p = 0.502).
Association of eGFR with disease activity: There was no association found between eGFR levels with disease activity. The correlation between eGFR and disease activity was not statistically significant (p = 0.545).
Association of eGFR with drugs used: We assessed whether there was any correlation between use of NSAIDs, prednisolone or both with eGFR level using the Chi square test and found no association between the drug used and eGFR level (p = 0.392).

Discussion

There is paucity of data on chronic kidney disease in rheumatoid arthritis. Majority of the studies have been undertaken in the developed countries and we were unable to access any studies done in Africa.

Whilst assessing eGFR, prevalence of CKD was found to be 27.5% as measured by an eGFR of less than 60ml/min/1.73m². This is a higher prevalence than that of the general African population whose prevalence of CKD is estimated to be 13.9%[11]. It would thus appear that patients with rheumatoid arthritis have an increased risk of CKD as compared to the general population.

When compared to other studies assessing CKD in patients with rheumatoid arthritis, the figures are much higher than 25.3% as noted by Karie *et al*[12], 12.75% by Daoussis *et al*[13] and 18% found by Hill *et al*[14] which are studies undertaken in Europe. The higher prevalence of CKD in our population may be explained by the fact that CKD is increased in blacks more than in their white counterparts[15]. This has in turn been attributed to genetic predisposition, low socio-economic status and inequities

in access to healthcare[16], factors which may apply to our population although this were not assessed by our study.

According to our findings, there were no patients with stage 5 CKD which could indicate that patients may be dying from other causes before their kidney disease worsens to end stage renal failure or their CKD is non-progressive in nature. Proteinuria is a strong indicator of disease progression in CKD. The absence of proteinuria among the study participants may support the postulation of the non-progressive nature of CKD in this population.

Proteinuria has been related to gold or penicillamine use both of which are not used in our setting. Proteinuria may also occur secondary to glomerulonephritis. The high prevalence of CKD in the absence of proteinuria may indicate a non-glomerular cause of CKD in this population. Glomerulonephritis in RA is now considered to be rare. Horak *et al*[17] notes it to be of little clinical significance and was only noted on either autopsy or biopsy in the past. Interestingly, the MATRIX study[12] also found an absence of patients with stage 5 CKD in their study population which may support the postulation that patients may either have a non-progressive disease or dying from other causes before progression to end-stage renal failure.

Another factor that may explain the lack of proteinuria in our study population is due to the fact that proteinuria is not recommended for CKD screening in a young population due to the low diagnostic yield[18].

Although our study set out to explore associations between CKD and various parameters, we were not powered to make significant conclusions out of these findings. Longitudinal studies may be better designed to assess for an association between disease duration and CKD.

Despite the significant use of NSAIDs and prednisolone (88.5%), either singly or in combination, it is worth noting that there was no association between NSAID or steroid use and CKD. The lack of correlation between the drugs used and kidney disease may be attributed to poor drug compliance by our study population although this was not assessed by this study.

Further studies are needed to ascertain the cause of high CKD prevalence in this population with longitudinal studies for determining disease progression.

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