RESEARCH ARTICLE

Cardiovascular risk factors in patients with rheumatoid arthritis at Kenyatta National Hospital

Kirui F, Oyoo GO, Ogola EN, Amayo EO

Department of Clinical Medicine and Therapeutics, School of Medicine, University of Nairobi, P. O. Box 19676 – 00202, Nairobi, Kenya

Corresponding author:
Dr GO Oyoo. Email: goyoo@uonbi.ac.ke / geomondi@hotmail.com

Abstract

Background: Rheumatoid arthritis is associated with excessive cardiovascular morbidity and mortality. This is predominantly due to accelerated coronary artery and cerebrovascular atherosclerosis. Traditional cardiovascular risk factors as well as extra articular disease have been associated with occurrence of myocardial infarction.

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

Design: This was a comparative cross sectional survey.

Setting: Kenyatta National Hospital medical outpatient clinic. The study population were patients with rheumatoid arthritis and the controls were individuals without RA age and sex matched staff of KNH. All those who consented were enrolled and a clinical evaluation was done as per the study protocol.

Results: One hundred patients with RA were screened out of which 80 were enrolled. The prevalence of hypertension among RA patients was 41.3%, diabetes 6.3%, dyslipidemia 71.3%, smoking 5%, obesity 22.5%, abnormal WHR 33.8%, family history of sudden death 5%, no family history of stroke or heart attack was reported. In the control group one hundred and five were screened and twenty five were excluded. The prevalence of hypertension was 22.5%, diabetes 5%, dyslipidemia 73.8%, smoking 2.5%, obesity 32.5%, abnormal WHR 33.8% family history of sudden death 10%, stroke 1.3% no history of heart attack was reported. Eighty percent of patients with RA were on at least one DMARD, 57.5% were on steroids and 37.5% were on NSAIDS.

Conclusion: There was a high prevalence of hypertension among RA patients (41.3%) than in the controls (22.5%) and this was statistically significant (OR 2.42 (95 CI 1.22-4.81) P = 0.017). Hypertension was also significantly associated with the use of DMARDS OR 2.189 (95% CI 1.111-4.312) P= 0.022 and steroids OR 2.06(95% CI 1.008-4.207) P= 0.022. No significant difference between patients with RA and controls in other risk factors including diabetes, dyslipidemia, smoking, obesity, abnormal waist hip ratio and family history of cardiovascular events was found.

Recommendations: Clinicians should keenly look out for hypertension in patients with RA for early identification and if necessary aggressive management of hypertension. Screening of cardiovascular risk factors in patients with RA should be done routinely and a larger study with normal controls from the general population should be undertaken in order to measure this cardiovascular risk factors and cardiovascular disease in this population.

Key words: Cardiovascular, Rheumatoid arthritis, Kenyatta National Hospital.

Introduction

Rheumatoid arthritis is a chronic systemic autoimmune inflammatory disorder. It is characterized by deforming symmetrical polyarthritis of varying extent and severity, associated with synovitis of joint and tendon sheaths. It is also associated with articular cartilage loss, erosion of juxta-articular bone and, in most patients, the presence of IgM rheumatoid factor in blood. In some patients systemic and extra-articular features may be observed during the course of the disease and, rarely prior to onset of joint disease. These include anemia, splenomegaly, 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[1] .

Rheumatoid arthritis (RA) is associated with excessive cardiovascular morbidity and mortality. This is predominantly due to accelerated coronary artery and cerebrovascular atherosclerosis. Traditional cardiovascular risk factors as well as extra articular disease have been associated with occurrence of myocardial infarction (MI) .

A study done by Han and colleagues[2], showed that individuals with rheumatoid arthritis are 30% to 60% more likely to suffer a cardiovascular event compared to the general population, especially myocardial infarction. The incidence and prevalence of stroke generally has been reported to be similar in rheumatoid arthritis as in the general population or in patients with osteoarthritis . One study found a higher prevalence of stroke in patients with rheumatoid arthritis than in controls[3].

The main objective of this study was to identify cardiovascular risk factors in patients with rheumatoid arthritis at Kenyatta National Hospital, Nairobi, Kenya. It also sought to determine the prevalence of hypertension, diabetes, dyslipidemia and smoking. We also wanted to determine anthropometric measures in patients with RA, mainly Basal Metabolic Index (BMI), Waist Hip Ratio(WHR), family history of cardiovascular events such as sudden death, MI or stroke. We also sought to compare the cardiovascular risk factors in patients with rheumatoid arthritis with the controls.

The other objectives in this study were to document cardiovascular events (stroke, MI, HF) in patients with RA and to document the use of DMARDS (disease modifying anti rheumatic drugs), steroids, NSAIDS, biologic DMARDS, anti-hypertensives, anti-diabetics, statins, and aspirin in patients with RA.

Materials and Methods

This was a descriptive comparative cross sectional survey done at the Medical Out Patient Clinics (MOPC) at Kenyatta National Hospital. Patients included in the study were above 18 years, confirmed to have rheumatoid arthritis as per ACR criteria and gave an informed consent. The controls were healthy individuals above 18 matched for age and sex. They were also confirmed not to have rheumatoid arthritis as per the ACR criteria. Patients below 18 years and those who declined to give consent were excluded.

Sample size was calculated based on the current data available with a prevalence of 30%[4] for hypertension at 95% confidence interval and a 5% margin of error. The minimum sample size needed was 80 with rheumatoid arthritis and 80 controls (Figure 1).

A total of 205 patients with rheumatoid arthritis and healthy controls were screened for recruitment into the study. Patients with or suspected to have RA were 100 and of these four individuals did not consent, 88 fulfilled ACR criteria and were recruited, 8 were lost to follow up and 80 were enrolled. One hundred and five healthy individuals without RA were screened for enrollment, 15 refused consent, 90 were recruited and 10 were lost to follow up. A total of 160 cases and controls were enrolled, 22 (13.75%) were males and 138 (86.25%) were female (Table 1).

Results

The mean age for patients with RA was 44.7 years, the median age 48 years and [range 18-75 years]. For the healthy individuals without RA, the mean age was 44.6 years, the median was 43 years and [range 22- 75 years] (Table 1). There were two peaks of disease in the patients with RA with the peaks at age ranges 20-29 and 50-59 years (Figure 2).

Figure 1: Flow chart showing patient flow in the study

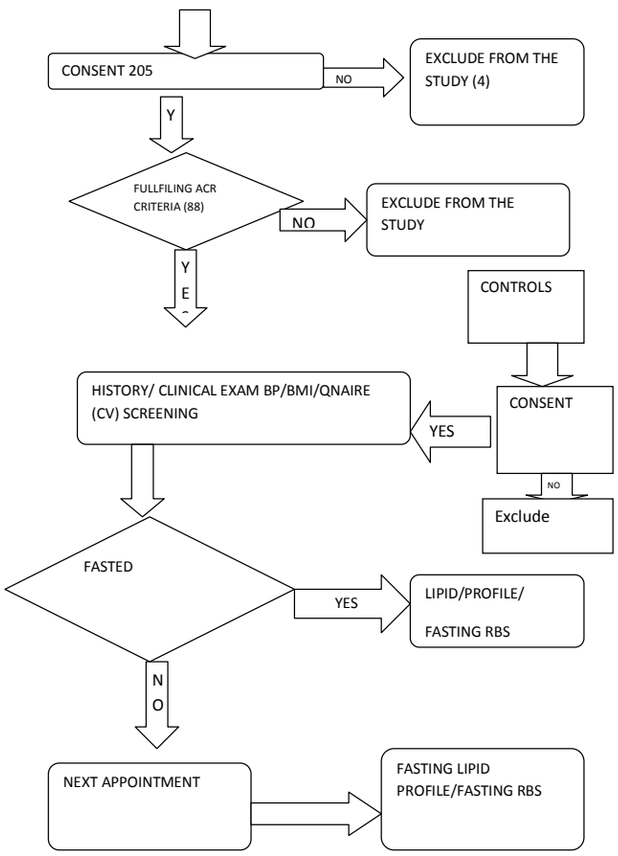
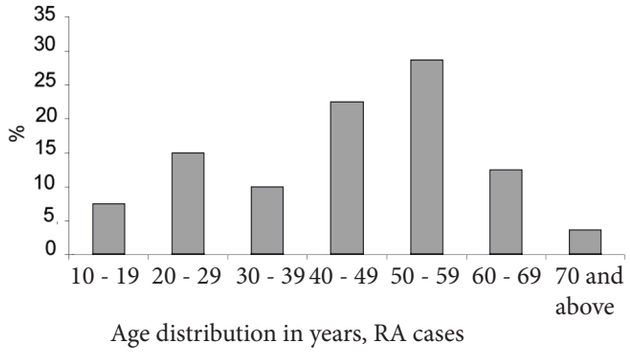


Table 1: Demographic characteristics of patients with rheumatoid arthritis and healthy controls

Variables/ categories	Case No. (%)	Control No. (%)	Total No. (%)	P value
Sex				
Male	11 13.8	11 13.8	22 13.8	1.000
Female	69 86.2	69 86.2	138 86.2	
Marital status				
Married	56 70	47 58.8	103 64.4	
Single	19 23.8	24 30	43 26.9	0.264
Widowed	3 3.8	8 10	11 6.9	
Divorced	2 2.5	1 1.3	3 1.9	
Level of education				
None	4 5	2 2.5	6 3.8	
Primary	28 35	10 12.5	38 23.8	
Secondary	15 18.7	9 11.3	24 15	<0.001
College	20 25	47 58.7	67 41.9	
Tertiary	13 16.3	12 15	25 15.6	
Employment				
Unemployed	24 30	20 25	44 27.5	
Employed	29 36.3	48 60	77 48.1	0.012
Self employed	19 23.7	8 10	27 16.9	
Retired	8 10	4 5	12 7.5	
Age				
Mean ±SD	44.7±15.3(18-75)	45.0± 13(22-75)	44.8 ± 14.2 (18 – 75)	0.894
Median	48	43	45	

There was significant association between level of education and rheumatoid arthritis (P= 0.001). Majority with education less than college level had higher disease burden compared to those who had college education and above. There was a significant association between type of employment and disease status. Majority of those who had rheumatoid arthritis were self employed, and unemployed (P = 0.012) (Table 1).

Figure 2: Age distribution of patients with rheumatoid arthritis



Thirty three patients (41.3%) with RA had hypertension compared to 18 (22.5%) healthy controls. This difference was statistically significant, (OR 2.42 (95 CI 1.22-4.81) P = 0.017) Five (6.3%) patients with rheumatoid arthritis had diabetes while controls were 4(5%) controls. This was not statistically significant (OR 1.28 (95 CI 0.33-4.90) P =1.0).

Fifty seven patients with RA (71.3%) had dyslipidemia, while 59(73.8%) of the healthy controls had dyslipidemia, however this was not statistically significant. (OR 0.88 (95 CI 0.44-1.77) P =0.723). Four (5%) patients with rheumatoid arthritis smoked and 2 (2.5%) healthy controls smoked cigarette. There was no statistical significance (OR 0.49 (95 CI 0.09-2.74) P =0 .687

Eighteen (22.5%) patients with rheumatoid arthritis were obese while 26 (32.5%) of the controls were obese. This was however not statistically significant. O.R 0.603 (95 CI 0.299-1.218) P =0.157. Twenty seven (33.7%) of patients with RA had a high waist hip ratio, a similar number was observed in the controls and this was not statistically significant. OR 1 (95 CI 0.519-1.926) P =1.0.

There was no family history of myocardial infarction among the patients with rheumatoid arthritis and the healthy controls, one person from the controls reported a family history of stroke. Four patients with RA reported a family history of sudden death while 8 people in the healthy control group did report it; however, when compared, this was not statistically significant. OR 0.47 95%CI (0.137-1.641) P = 0.369. Only one patient with RA reported past history of heart failure; none of the patients or healthy controls reported a previous history of myocardial infarction or stroke. Drug therapy as used by all the patients is summarized in Table 2.

Table 2: Drug therapy in patients with RA and controls

Characteristic	Cases		Controls	
	No.	(%)	No.	(%)
Drugs				
Steroids	46	57.5	0	0
Statins	1	1.3	2	2.5
Nitrates	0	0	0	0
Aspirin	1	1.3	3	3.8
DMARDS	64	80	0	0
Biological DMARDS	0	0	0	0
NSAIDS	30	37.5	6	7.5
Proportion of hypertensive patients on medication	8	24.2	1	5.5
Proportion of diabetics on treatment	3	60	2	50

Data Analysis

Table 3: Bivariate analysis on correlates of cardiovascular risk factors in patients with rheumatoid arthritis and healthy controls

Factors	Category	Disease outcome				P. value	OR	CI OR
		Case		Control				
		No.	(%)	No.	(%)			
Hypertension		33	41.3	18	22.5	0.017	2.42	1.22 - 4.81
Diabetes		5	6.3	4	5	1	1.27	0.33 - 4.90
Smoking		4	5	2	2.5	0.681	0.49	0.09 - 2.74
Abnormal WHR		27	33.8	27	33.8	1	1	0.52 -1.93
Sudden death		4	5	8	10	0.369	0.474	0.14 - 1.64
Dyslipidemia		57	71.3	59	73.8	0.723	0.882	0.440 -1.767
BMI		18	22.5	26	32.5	0.157	0.603	0.299 - 1.218

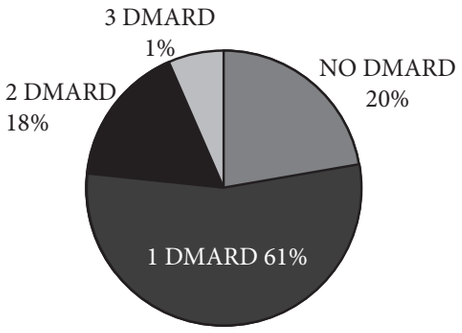
By controlling for disease outcome 19 (44.2%) patients with RA and obesity were hypertensive, however there was no statistically significance between hypertension and obesity. Likewise in the control group there was no association between hypertension and obesity. OR 1.96 (95 C I 0.67 -5.76) P = 0.259. The controls who were obese were almost two times more at risk to have hypertension than those not obese. One patient with RA and diabetes (20%) was hypertensive, while two controls who were diabetic had hypertension. The odds of being hypertensive among diabetics compared to non diabetic was three times more, however this was not statistically significant OR 3.75(95% C.I 0.490-28.727) P= 0.217. Twelve (40%) individuals with RA who used NSAIDS regularly were hypertensive while one control had hypertension; however this was not statistically significant (Table 4).

Table 4: Bivariate analysis –Controlling for disease status

	Disease outcome Case No.	(%)	Control No.	(%)	Case 95% CI	P value	Control 95% CI	P value
Hypertension/Obesity	8	24.2	8	44.4	1.2 (0.41-3.42)	0.791	1.96 (0.67 - 5.76)	0.259
Hypertension/Diabetes	1	20	2	50	0.34(0.04-3.15)	0.399	3.75 (0.49-28.7)	0.217
Hypertension/NSAIDS	12	40	1	16.7	0.92 (0.37-2.3)	1	0.67(0.73-6.14)	1

Among the patients with rheumatoid arthritis 64 (80%) were on DMARDS, 49 (61.3%) were on one DMARD, 14 (17.5%) were on two DMARDS and only one patient with rheumatoid arthritis was on treatment with three DMARDS. (Figure 3).

Figure 3: Use of DMARDS among individuals with rheumatoid arthritis



more likely to be hypertensive than the controls and this was statistically significant OR 2.06(95% CI 1.008-4.207) P= 0.022 (Table 5).

Forty six (57.5%) individuals with RA were on treatment with steroids. Only one patient with rheumatoid arthritis was on treatment with statins while two controls were using statins. Only one patient with RA who was using antiplatelet agent while three controls were on antiplatelet agents. None of the cases or controls was on treatment with nitrates.

Eight (24.2%) individuals who had RA and hypertension were on treatment for hypertension while three (60%) individuals were on treatment for diabetes. Thirty (37.5%) individuals with RA were taking NSAIDS

Table 5: Hypertension in relation to drug therapy in patients with RA and controls

Variables/ category	Hypertension No.	(%)	No Hypertension No.	(%)	O. R	95% O.R Lower	Upper	P value
Use of DMARDS	27	42.2	37	57.8	2.189	1.111	4.312	0.022
No use of DMARDS	24	25.0	72	75.0				
Use of steroids	20	43.5	26	56.5	2.06	1.008	4.207	0.045
No use of steroids	31	27.2	83	72.8				
Use of NSAID	13	36.1	23	63.9	1.279	0.586	2.79	0.536
No use of NSAID	38	30.6	86	69.4				

None of the patients seen at the clinic were using biological agents for the treatment of rheumatoid arthritis (Table 2).

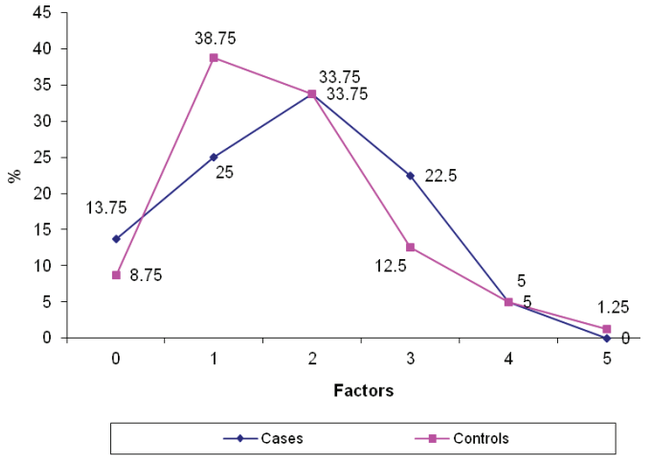
Twenty seven patients who used DMARDS were hypertensive as compared to 24 who did not. Those who used DMARDS were significantly more likely to have hypertension. OR 2.189(95% CI 1.111-4.312) P= 0.022. Likewise those patients with RA who used steroids were

regularly as compared to six individuals in the control group. Among the individuals with RA taking NSAIDS regularly 12(40%) were hypertensive. More than half the patients with rheumatoid arthritis 46(57.5%) were using glucocorticoids (Table 2).

Eleven patients with RA had no risk factor measured in this study, 20 patients had 1 risk factor, 27 two risk factors, 18 three risk factors and 4 with four risk factors.

In the control arm 7 did not have any risk factor, 31 had 1 risk factor, 27 two risk factors, 10 three risk factors, 4 had four risk factors and 1 with five risk factors. When the cases and controls were compared there was no statistical significance in terms of number of risk factors.

Figure 4: Distribution of risk factors by cases and controls



Discussion

From our results we found women were the most affected by the disease accounting for 69(86.2 %) of the individuals with RA, as opposed to eleven (13.8%) males. A local study done by Owino *et a l*[5] found 86.7% females with a male to female ratio of 1:6.5. This observation was in agreement to what we observed in our study.

The mean age of patients with RA in this study was 44.7 ± 15.3 years and this was almost similar to that observed by owino *et al*[5] but older than that observed by Bagg *et al* [6]. In the study done by panoulas and colleagues[7] the mean age for patients with RA was 61 ± 12.02 years. This was an older population than what we saw in our study and could explain our higher prevalence of rheumatoid arthritis among women, since the disease has been shown to be more common in younger women compared to younger males; but the difference diminishes as the age increases.

In this study the prevalence of hypertension among the patients with rheumatoid arthritis was 41.3%, and this was higher than the 22.5% observed in the healthy controls and was statistically significant.

Owino *et al*[5] found the prevalence of hypertension among patients with rheumatoid arthritis to be around 14%. This was much lower than what we observed in our study. The mean age of his patients was 41.3 years indicating a younger population than in ours. This may partly explain the lower prevalence although other factors might have contributed to the difference observed. Owino and his colleagues[5] relied on patient's records and there was no physical measurement by the clinician or study assistant of blood pressure and this may partly explain the low prevalence he got from his study.

A study done by panoulas *et al* [7] in the UK found a higher prevalence of 70% with a mean age of 62 years. This population was older than our study population and it has been shown that hypertension is more common in older age group[8] of individuals. The prevalence of hypertension might have been also high in Panoulas study population and this with the high mean age might explain the difference with our study.

Use of medium dose steroids for long term (more than six months) in patients with RA has been associated with a high prevalence hypertension[9] . In this study 46 (57.5%) patients with RA were on steroids out of which 20(43.5%) had hypertension. Those who used steroids were twice at risk of being hypertensive than those who did not use and this was statistically significant. We did not document the daily steroid use in our study and therefore would not have a daily steroid dose to correlate with other studies findings. The use of steroids in patients with RA could explain the higher prevalence of hypertension in this patient group compared to the controls. The study done by Owino and colleagues[5] had 66.7% of patients with RA on steroids; which was much higher than in our study but this cannot explain the difference in the prevalence of hypertension, probably other factors could explain this observation.

Antonio *et al* [4] found 33% of patients with RA had hypertension. This was a multicentre study and involved different geographical and demographic groups globally but mostly in Europe and North America. This prevalence of hypertension was lower than what we observed in our study. Their mean age was 57 years. These findings were not in agreement with what has been observed in other studies, our study included.

Only 24.2 % of the individuals with rheumatoid arthritis and hypertension were on treatment for hypertension in our study, and this shows a significant proportion of individuals are not diagnosed with hypertension and therefore could not benefit from early treatment. Panoulas and colleagues[7] observed that 39.4% of the individuals with RA were undiagnosed for hypertension and therefore could not get treatment in his study. This is despite the fact that patients with RA in that country (UK) were regular attendees of the rheumatology clinics where vital signs were recorded regularly.

In our study the prevalence of diabetes was 6.5% among patients with rheumatoid arthritis and 5% in the controls. In a study done by Owino[5] 3.5% of individuals were diabetic and hypertensive. Other studies like the one done by Antonio and his colleagues[4] observed a prevalence of diabetes of 8%. This was a multicentre study and had varied demographic characteristics although 90% of the patients were Caucasians and they had a higher mean age than in our study. Another study done by Del Rincon *et al*[10], found a prevalence of 8.3% of diabetes among patients with RA and 6.3% in his controls, however, this was not statistically significant. This finding was observed in patients and controls below 55 years of age. He did observe a higher prevalence in those who were above 55 years. The patients in his study were older than in our study and this could explain the higher prevalence

he observed in his study or probably the prevalence of diabetes was higher in his study population. Steroids have been shown to predispose patients to diabetes [11] and we may associate to the higher prevalence of diabetes in patients with RA in our study since over half (57.5%) of them were on steroids.

Fifty seven (71.3%) of our patients with RA had dyslipidemia and almost a similar number was observed in the control group. We have no local data on dyslipidemia among patients with RA. This was higher than what was observed by Antonio and his colleagues[4] (14%). The low prevalence observed by Antonio and colleagues could have been due to the difference in the cut off levels for lipid profiles or their definition of dyslipidemia.

Crowson *et al*[12] observed a higher prevalence of dyslipidemia in his study (59.4%). This was a study done in the US looking at risk of developing heart failure attributable to traditional cardiovascular risk factors in patients with RA. A small proportion of our patients with Rheumatoid arthritis smoked, likewise this trend was observed in the healthy controls. This low prevalence might have been influenced by the cultural trends in our society since majority of the study population were women. Older women in the Kenyan society tend to be conservative and therefore few of them smoke, although of late the trend of smoking has been seen to be rising among young women in Kenya.

Our findings were in sharp contrast to what was seen in the quest RA study where the prevalence of ever smoking was at 43%. These could be explained by the population studied in Quest RA study which was more of a western society where a significant proportion of women smoke cigarettes. Panoulas *et al* observed a prevalence of 18.5% of smoking in his study and these was still higher than what we saw in our study.

Obesity particularly central obesity is associated with an increased risk of cardiovascular risk [13]. In our study the prevalence of obesity among patients with rheumatoid arthritis was 22.5% compared to 32.5% in the controls. Antonio and his colleagues[4] in the quest RA study found a lower prevalence of 18% . Patients with RA tend to present with weight loss when the disease is active and while on treatment and this might explain the difference we got from our study when we compared our cases and the controls. Other studies in the general population have shown that overweight and obese are important mediators of hypertension in the context of ex smokers with insulin resistance (Yokoyama 2004)[1], and associate with current or future hypertension and relevant end organ damage in non RA population.

The number of individuals with RA using DMARDS was 64(80%) in our study. Owino *et a l*[5] observed that 46.7% of patients with RA were on treatment with at least one DMARD these was lower than what we observed in our study. We think that there could have been some improvement in knowledge of the healthcare workers in the use of DMARDS in patients with RA and therefore more people are being put on DMARDS now than before, or may be DMARDS are now more affordable. A study done by Panoulas *et al* [7] found out that 87.5% of patients with RA were using DMARDS. This was higher than what we found in our study although the trend was almost similar with over two thirds of our patients with RA using DMARDS.

In our study in patients with RA; 61.3% were on one DMARD, 17.5% on two DMARDS and one 1.3% on three DMARDS as compared to the ones in a study done by Panoulas *et al*[7] where 56.8% of patients with RA were on only one DMARD. This was lower than what we observed in our study, the reason being that more patients were on more than one DMARD (30.8%) in that study. These might reflect on our local practice because in other parts of the world rheumatologist are increasingly prescribing combination therapy [14] because single DMARD therapy often fails to control clinical symptoms or prevent disease progression.

The use of NSAIDS especially Cox 2 inhibitors [15] have been associated with hypertension , unlike in our study where there was no significant association of hypertension and use of NSAIDS. None of the patients in our study were using biological agents such as Rituximab, which has been shown to be quite effective in treating RA. This is most likely due to its prohibitive cost and also most of the patients coming to Kenyatta Hospital have a lower socio economic status.

The family history of documented cardiovascular events was lower than that observed by Crowson *et al*[12] in the US. There could have been recall bias among our patients on current disease or their social desirability might have influenced their response. Recording and maintaining updated records of this information in our local set up might have posed a significant challenge and this might explain the low prevalence we got from our study.

Most of the controls in our study were individuals working at the hospital. They included the nursing staff, clinical officers and supportive staff, a large proportion of them had dyslipidemia (73.8%) and this was more than in the cases. Although this was not statistically significant it still shows that this population was at risk. The healthy individuals who were used as controls were also more obese (32.5%) than the patients with RA indicating that they were at more risk, although this was also not statistically significant. They also documented more family history of sudden death than in the cases with RA. From our findings it seems the control group which was presumed healthy had actually more risk factors than thought and these might have influenced our results especially looking at the lipid profile where we expected to have more dyslipidemia in patients with RA than in the controls as seen in a study done by Situnayake and kitas.

Most of the patients and controls had clustering of risk factors and when the two groups were compared there was no significance in the number of risk factors. It seems the increased risk of cardiovascular events in RA is independent of traditional cardiovascular risk factors. This suggests other additional mechanisms are

responsible for cardiovascular disease in RA and further research needs to be done.

Conclusions

This study has shown that;

(i)There is a high prevalence of hypertension in patients with RA as compared to the controls.

(ii)Hypertension was also associated with the use of DMARDS and steroids.

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

(iv) There was no significant difference between patients and controls in terms of other risk factors i.e. diabetes mellitus, dyslipidemia, smoking, BMI, WHR, and family history of cardiovascular events.

(v) There was clustering of risk factors among patients and the healthy controls although this was not significant. From this it seems the increased risk of cardiovascular events in RA is independent of traditional cardiovascular risk factors. This suggests other additional mechanisms are responsible for cardiovascular disease in RA.

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