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

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KEMRI/WRP HIV PROGRAM – KERICHO
EPIDEMIOLOGY

- Rheumatoid arthritis (RA) is a disease that is observed worldwide and affects all races. Women are affected X3 more often than men.

- Prevalence APPROX- 0.8%(0.3-1.2%) globally (1)

- SA black popn -Approx (0.2%-1%), (2)
- Kenya Owino et al-60 pts (6Months)

RA and cardiovascular disease (CVD)

- RA is associated with increased mortality, which is predominantly due to accelerated coronary artery & cerebrovascular atherosclerosis -occurs in established/ early RA

- Accelerated atherosclerosis is due to indirect effect of inflammation centered on the synovium, acting at a distance on the systemic vascular endothelium


Intro cont  RA and CVD

- Cardiovascular (CV) events occur approx a decade earlier in RA than in the gen popn, suggesting that RA, similarly to DM, is an independent risk factor (RF) for premature IHD.

- QUEST RA study(4) showed that all traditional CV RFs except obesity and physical inactivity were significantly associated with CV morbidity.

- Han & colleagues, showed that individuals with RA are 30% to 60% more likely to suffer a CV event compared to the general popn, especially MI. He also found a higher prev of stroke in pts with RA.


Hypertension has also been shown to be very common in pts with RA, under diagnosed particularly in the young & under treated particularly in the old RA patients with CVD(6).

The adjusted RR of MI in women with RA compared to those without RA is estimated to be around 2.0 (6).

NSAIDs, COXII inhibitors, oral steroids & DMARDs( leflunomide /cyclosporin)may cause major or minor increments inBP(7)

Individuals who smoke are more likely to develop RA & more likely to have a more severe disease (8).

Use of methotrexate has been associated with a significantly lower risk for CV events in RA patients (9).


JUSTIFICATION OF STUDY

- RA is associated with a lot of morbidity & mortality due to CVD. This is predominantly due to accelerated coronary artery and cerebrovascular atherosclerosis. It has also been shown that there is a high prevalence of traditional CV risk factors in pts with RA.

- This cardiovascular events have been known to occur a decade earlier in pts with RA than in the gen popn. We do not have local data documenting on burden of traditional CV risk factors in our popn with RA.

- This was a baseline study that will address this issues & will guide us in formulating strategies for intervention of these risk factors in our local popn with RA.
OBJECTIVES

General Objectives
☐ To identify traditional cardiovascular risk factors in patients with RA at KNH

Specific objectives
1 To determine prevalence of Hypertension,
2 Dysglycaemia,
3 Dyslipidaemia
4 Smoking,
5 Anthropometric measurements,
6 Family HX of CV events such as sudden death, MI or stroke in RA
7 To compare the CV Risk factors in pts with RA with the controls

Secondary objectives
1 To document CV events (stroke, MI, HF) in pts with RA
2 To document the use of DMARDs, steroids, NSAIDS, biologic DMARDs, anti-hypertensive, anti-diabetic medication, statins, & aspirin in pts with RA.
METHODOLOGY

- **Study design**
  This was a descriptive comparative cross sectional survey.

- **Study site**—The study site was MOPC at Kenyatta National Hospital

- **Study population**
  Pts above 18 years clinically diagnosed to have RA according to ACR criteria attending MOPC at KNH. The controls were individuals without RA (Healthy staff from KNH (nurses, clinicians, support staff).

  **Inclusion criteria for RA cases**
  - Above 18 years
  - Confirmed to have RA as per ACR criteria
  - Willing to participate and sign an informed consent

  **For the controls**
  - Individuals above 18 age and sex matched
  - Confirmed not to have RA as per ACR criteria
SCREENING AND RECRUITMENT

5.6.1 Clinical procedures
- Consent on patients meeting the ACR criteria. Baseline demographic & socio-economic data was collected using standardized questionnaires.
- A detailed review of their medical history and hospital records, physical examination, and contemporary assessments of height, BP, weight, WHR. BMI was obtained. All medications and their exact indication was recorded.

Controls
- Individuals who were not having RA age and sex matched.

Lab procedures
The patients/controls then had blood drawn fasting blood sugar/fasting lipid profile.
Variables

- **Waist Circumference**
  - Central Obesity is defined according to the NCEP / ATP III by a waist circumference of \( \geq 102 \text{cm} \) in males and \( \geq 88 \text{ cm} \) in females.

- **Waist Hip Circumference Ratio**
  - Defined by WHO criteria as abnormal if the ratio \( >0.90 \) in males and \( >0.85 \) in females.

- **Use of Alcohol**
  - Never
  - Current (quantity and duration defined)
  - Former (Period of abstinence defined)

- **Smoking**
  - Never smoked
  - Current smoker - pack years defined
  - Former smoker - period of abstinence defined.
Variables cont /Data management /IRB

Dyslipidaemia

- Serum LDL Cholesterol > 2.58mmol/L, HDL Cholesterol <1.03mmol/L , Total Cholesterol > 5.17mmol/L , Triglycerides > 2.26mmol/L
- Anyone with abnormalities in any of the above parameters had dyslipidemia

Diabetes - Fasting glucose > 7mmol/l / or on oral hypoglycemic / insulin
- A Pt with symptoms of; diabetes and a RBG > 11.1 mmol/L.

Obesity and BMI classification
- Those who were obese had a BMI > 30

DATA MANAGEMENT AND ANALYSIS

- All data was collected entered into MS ACCESS and analysis was performed using SPSS version 15.0 software.

IRB approval

- Dept Medicine UON & KNH Ethical Review board
Pts Suspected to have RA

- Consent
  - Yes
    - Fulfilling ACR criteria
      - Yes
        - Hx/Exam/BP/Qnaire/
          - Yes
            - Fasted
              - No
                - Next appointment
              - Yes
                - Lipid/FBS
          - No
            - Exclude from study
      - No
        - Exclude from study
  - No
    - Exclude from study

- Fasting lipid/FBS
RESULTS

Cases

- 100
- 4 Refused consent
- 96
- 8 not fulfilled ACR criteria
- 88 fulfilled ACR criteria
- 8 lost to follow up
- 80 enrolled

Controls

- 105
- 15 Refused consent
- 90
- 10 lost to FU
- 80 enrolled
Demographic characteristics of patients with Rheumatoid Arthritis and healthy controls

<table>
<thead>
<tr>
<th>Variables/ categories</th>
<th>Case n (%)</th>
<th>Control n (%)</th>
<th>Total n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11(13.8)</td>
<td>11(13.8)</td>
<td>22(13.8)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>69(86.2)</td>
<td>69(86.2)</td>
<td>138(86.2)</td>
<td>1</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>56(70)</td>
<td>47(58.8)</td>
<td>103(64.4)</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>19(23.8)</td>
<td>24(30)</td>
<td>43(26.9)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>3(3.8)</td>
<td>8(10)</td>
<td>11(6.9)</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>2(2.5)</td>
<td>1(1.3)</td>
<td>3(1.9)</td>
<td>0.264</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4(5)</td>
<td>2(2.5)</td>
<td>6(3.8)</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>28(35)</td>
<td>10(12.5)</td>
<td>38(23.8)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>15(18.7)</td>
<td>9(11.3)</td>
<td>24(15)</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>20(25)</td>
<td>47(58.7)</td>
<td>67(41.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tertiary</td>
<td>13(16.3)</td>
<td>12(15)</td>
<td>25(15.6)</td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>24(30)</td>
<td>20(25)</td>
<td>44(27.5)</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>29(36.3)</td>
<td>48(60)</td>
<td>77(48.1)</td>
<td></td>
</tr>
<tr>
<td>Self employed</td>
<td>19(23.7)</td>
<td>8(10)</td>
<td>27(16.9)</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>8(10)</td>
<td>4(5)</td>
<td>12(7.5)</td>
<td>0.012</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>45.0±13(22-75)</td>
<td>14.2 (18)</td>
<td>0.894</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>44.7±15.3(18-75)</td>
<td>43</td>
<td>45</td>
<td></td>
</tr>
</tbody>
</table>
# Cardiovascular risk factors in patients with RA & healthy controls

<table>
<thead>
<tr>
<th>Factors</th>
<th>Category</th>
<th>Disease outcome</th>
<th>P.value</th>
<th>O.R</th>
<th>C.I O.R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td>33(41.3%)</td>
<td>18(22.5%)</td>
<td>0.017</td>
<td>2.42</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>5(6.3%)</td>
<td>4(5%)</td>
<td>1</td>
<td>1.27</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td>4(5%)</td>
<td>2(2.5%)</td>
<td>0.681</td>
<td>0.49</td>
</tr>
<tr>
<td>Abnormal WHR</td>
<td></td>
<td>53(66.3%)</td>
<td>53(66.3%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Sudden death</td>
<td></td>
<td>4(5%)</td>
<td>8(10%)</td>
<td>0.369</td>
<td>0.474</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
<td>57(71.3%)</td>
<td>59(73.8%)</td>
<td>0.723</td>
<td>0.882</td>
</tr>
<tr>
<td>BMI &gt; 30</td>
<td></td>
<td>18(22.5%)</td>
<td>26(32.5%)</td>
<td>0.157</td>
<td>0.603</td>
</tr>
</tbody>
</table>
Use of DMARDS among individuals with rheumatoid arthritis

- 1 DMARD: 61%
- 2 DMARDS: 18%
- 3 DMARDS: 1%
- NO DMARD: 20%

1 DMARD: 61%
2 DMARDS: 18%
3 DMARDS: 1%
NO DMARD: 20%
### Table 2: Drug therapy in patients with RA and Controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases N</th>
<th>%</th>
<th>Controls N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drugs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td>46</td>
<td>57.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Statins</td>
<td>1</td>
<td>1.3</td>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>Nitrates</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1</td>
<td>1.3</td>
<td>3</td>
<td>3.8</td>
</tr>
<tr>
<td>DMARDS</td>
<td>64</td>
<td>80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biological DMARDS</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>30</td>
<td>37.5</td>
<td>6</td>
<td>7.5</td>
</tr>
<tr>
<td>Proportion of Hypertensive pts on medication</td>
<td>8</td>
<td>24.2</td>
<td>1</td>
<td>5.5</td>
</tr>
<tr>
<td>Proportion of Diabetics on treatment</td>
<td>3</td>
<td>60</td>
<td>2</td>
<td>50</td>
</tr>
</tbody>
</table>

Only 1 pt with RA reported past HX of Heart failure; none of the pts with RA/controls reported a previous history of MI or stroke.
### Table 5: Hypertension in relation to drug therapy patients with RA and controls

<table>
<thead>
<tr>
<th>Variables/ category</th>
<th>Hypertension</th>
<th>No Hypertension</th>
<th>O. R</th>
<th>95% O.R</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>Lower</td>
</tr>
<tr>
<td>Use of DMARDs</td>
<td>27</td>
<td>42.2</td>
<td>37</td>
<td>57.8</td>
<td>2.189</td>
</tr>
<tr>
<td>No use of DMARDs</td>
<td>24</td>
<td>25.0</td>
<td>72</td>
<td>75.0</td>
<td>2.06</td>
</tr>
<tr>
<td>Use of steroids</td>
<td>20</td>
<td>43.5</td>
<td>26</td>
<td>56.5</td>
<td>2.06</td>
</tr>
<tr>
<td>No use of steroids</td>
<td>31</td>
<td>27.2</td>
<td>83</td>
<td>72.8</td>
<td></td>
</tr>
<tr>
<td>Use of NSAID</td>
<td>13</td>
<td>36.1</td>
<td>23</td>
<td>63.9</td>
<td>1.279</td>
</tr>
<tr>
<td>No use of NSAID</td>
<td>38</td>
<td>30.6</td>
<td>86</td>
<td>69.4</td>
<td></td>
</tr>
</tbody>
</table>
Table 6: Proportion of patients with RA and controls and the number of risk factors.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>8.75</td>
<td>13.75</td>
</tr>
<tr>
<td>1</td>
<td>13.75</td>
<td>38.75</td>
</tr>
<tr>
<td>2</td>
<td>33.75</td>
<td>33.75</td>
</tr>
<tr>
<td>3</td>
<td>22.5</td>
<td>12.5</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>1.25</td>
<td>0</td>
</tr>
</tbody>
</table>

R0=11.7; R1=20.31; R2=27.27; R3=18.10; R4=4.4; R5=0.1

P = 0.257
5.1: Discussion

- In this study, women were the most affected - 69 (86.2%) - 11 (13.8%) males. Agree with Owino et al study - 86.7% F, Panoulas et al 73%

- Mean age - 44.7 ± 15.3, almost similar to that observed by Oyoo et al.
- Prevalence of HTN in pts with RA was 41.3%, controls (22.5%) significant.
  - Owino et al 14% - younger popn, methodology
  - Panoulas et al - 70%, mean age - 62
  - Antonio et al 33%, mean age - 57

- 46 (57.5%) of pts with RA were on steroids & 20 (43.5%) had HTN

- Only 24.2% of the individuals with RA & HTN were on RX for HTN in our study

- Prevalence of DM was 6.5% among pts with RA
  - 3.5% by Owino et al.
5.2 Conclusions

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

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

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

- There was clustering of risk factors among patients and the healthy controls although this was not significant. From 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.
5.3 Recommendations

- 1) Clinicians should keenly look out for hypertension in patients with RA for early identification and if necessary aggressive management of the hypertension.

- 2) People on steroid therapy should be closely monitored for high blood pressure and screened for diabetes

- 3) Screening for cardiovascular risk factor should be routinely done and a larger study with normal controls from the gen popn should be undertaken.
5.4 Study limitations

- 1) BP measurement - on the spot BP may not be a true reflection of pts BP. We needed to rule out “white coat” HTN. Ideally 2 or more clinic visits was needed.

- 2) Recall bias - Recollection of some historical factors may have been biased based on either their current dse state or social desirability. Under or over – estimation of the significance of a RF

- 3) Recall bias with regard to symptoms of acute MI, pts may not remember having had the symptoms.

- 4) Selection bias: Those enrolled were pts only referred to KNH

- 5) This was a cross sectional study has limitations - causality cannot be proven
Acknowledgements

- Patients at KNH MOPC with RA
- Staff at KNH
- Professor E Ogola
- Professor AMAYO
- Dr Omondi Oyoo
- KEMRI
THANK YOU!