Baseline characteristics and outcome of rheumatic heart disease in REMEDY: clinical and policy implications

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University of Cape Town
Clinical and policy indicators
Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study)
Global Rheumatic Heart Disease Registry: *REMEDY*

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egypt</td>
<td>2</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>2</td>
</tr>
<tr>
<td>India</td>
<td>2</td>
</tr>
<tr>
<td>Kenya</td>
<td>1</td>
</tr>
<tr>
<td>Malawi</td>
<td>1</td>
</tr>
<tr>
<td>Mozambique</td>
<td>2</td>
</tr>
<tr>
<td>Namibia</td>
<td>1</td>
</tr>
<tr>
<td>Nigeria</td>
<td>5</td>
</tr>
<tr>
<td>South Africa</td>
<td>3</td>
</tr>
<tr>
<td>Sudan</td>
<td>2</td>
</tr>
<tr>
<td>Rwanda</td>
<td>1</td>
</tr>
<tr>
<td>Uganda</td>
<td>1</td>
</tr>
<tr>
<td>Yemen</td>
<td>1</td>
</tr>
<tr>
<td>Zambia</td>
<td>1</td>
</tr>
</tbody>
</table>

Karthikeyan, Zuhlke, Engel et al 2012 AHJ
## Enrolled sites in income groups

<table>
<thead>
<tr>
<th>Low income countries</th>
<th>Lower middle income countries</th>
<th>Upper middle income countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n 1110, 33.2%)</td>
<td>(n 1370, 41%)</td>
<td>(n 863, 25.8%)</td>
</tr>
<tr>
<td>Ethiopia (n 400)</td>
<td>Egypt (n 286)</td>
<td>Namibia (n 266)</td>
</tr>
<tr>
<td>Kenya (n 316)</td>
<td>India (n 293)</td>
<td>South Africa (n 654)</td>
</tr>
<tr>
<td>Malawi (n 37)</td>
<td>Mozambique (n 41)</td>
<td></td>
</tr>
<tr>
<td>Rwanda (n 5)</td>
<td>Nigeria (n 199)</td>
<td></td>
</tr>
<tr>
<td>Uganda (n 311)</td>
<td>Sudan (n 175)</td>
<td></td>
</tr>
<tr>
<td>Zambia (n 116)</td>
<td>Yemen (n 301)</td>
<td></td>
</tr>
</tbody>
</table>

Zuhlke, Engel et al Eur Heart Journal
## Results

<table>
<thead>
<tr>
<th>Participants</th>
<th>3 433</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median [IQR]</td>
<td>28 [18-40]</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>2 211 (66.2)</td>
</tr>
<tr>
<td>Women in childbearing age (12-51) , n (%)</td>
<td>1 825 (54.6)</td>
</tr>
<tr>
<td>Children (up to 18 years), n (%)</td>
<td>921 (27.6)</td>
</tr>
<tr>
<td>Adults with no formal education, n (%)</td>
<td>458 (19.1)</td>
</tr>
<tr>
<td>Unemployed adults, n (%)</td>
<td>1 815 (75.3)</td>
</tr>
</tbody>
</table>
### Age and Gender Distribution

**Total group n=3343**

- **Children < 18 years n=941**
  - 34% Male
  - 66% Female

- **Total group n=3343**
  - 54% Male
  - 46% Female

#### Age categories

- **Low income countries N=1110 (33.2%)**
  - Median age[IQR] 24[15-34]
  - Women in childbearing age 630(86.5%)

- **Lower middle income countries N=1370 (41.0%)**
  - Median age[IQR] 28[18-38]
  - Women in childbearing age 783(90.3%)

- **Upper middle income countries N=863 (25.8%)**
  - Median age[IQR] 39[22-52]
  - Women in childbearing age 412(66.9%)

<table>
<thead>
<tr>
<th>Income Level</th>
<th>Median age[IQR]</th>
<th>Women in childbearing age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low income</td>
<td>24[15-34]</td>
<td>630(86.5%)</td>
</tr>
<tr>
<td>Lower middle</td>
<td>28[18-38]</td>
<td>783(90.3%)</td>
</tr>
<tr>
<td>Upper middle</td>
<td>39[22-52]</td>
<td>412(66.9%)</td>
</tr>
</tbody>
</table>

**P values:**
- Median age[IQR] 0.4
- Women in childbearing age 0.01
## Reproductive health services

<table>
<thead>
<tr>
<th>Category</th>
<th>Women n=2211 (66.2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women in childbearing age</td>
<td>1825 (82.5%)</td>
</tr>
<tr>
<td>Severe mitral stenosis</td>
<td>416 (45.8%)</td>
</tr>
<tr>
<td>Prosthetic valves</td>
<td>280 (15.3%)</td>
</tr>
<tr>
<td>Contraception</td>
<td>65 (3.6%)</td>
</tr>
<tr>
<td>Pregnant</td>
<td>73 (4.0%)</td>
</tr>
<tr>
<td>On Warfarin</td>
<td>15 (20.5%)</td>
</tr>
</tbody>
</table>
Findings on history and clinical examination

<table>
<thead>
<tr>
<th>Condition</th>
<th>Low income countries N=1110(33.2%)</th>
<th>Lower middle income countries N=1370(41.0%)</th>
<th>Upper middle income countries N=863(25.8%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>58(5.2%)</td>
<td>52(3.8%)</td>
<td>125(14.5%)</td>
<td>0.0068</td>
</tr>
<tr>
<td>CVS *</td>
<td>96 (8.7)</td>
<td>137 (10.1)</td>
<td>191 (22.2)</td>
<td>0.0281</td>
</tr>
</tbody>
</table>

*Cardiovascular complications include any of the following events: stroke, infective endocarditis, major bleeding, or peripheral embolism;
Echocardiography

Participants n=3343

<table>
<thead>
<tr>
<th>Condition</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased LV Ejection Fraction (children)</td>
<td>168 (5.3%)</td>
</tr>
<tr>
<td>Decreased LV Ejection Fraction (adults)</td>
<td>661 (26.5%)</td>
</tr>
<tr>
<td>Increased LV End-Diastolic Diameter (children)</td>
<td>454 (14.1%)</td>
</tr>
<tr>
<td>Increased LV End-Diastolic Diameter</td>
<td>742 (23%)</td>
</tr>
</tbody>
</table>

Percentage Valve involvement

- Single Valve: 35%
- Two Valves: 44%
- Three Valves: 19%
- Quadrivalvar disease: 2%


AHA/ACC Guidelines Circulation 2014; 129(23):
• Our patients are young, largely female and generally severely affected.

• Women should have pre-pregnancy counseling and referred to reproductive services/combined cardio-obstetric clinics when available.
Indications for and use of Warfarin

- 65% Yes
- 35% No

Atrial fibrillation
Chaotic activity in atria

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Warfarin

INR tests in past 6 months

- None: 15%
- 1-3: 11%
- 4-6: 34%
- More than 6: 40%

Enrolment INR

- Mechanical Valves:
  - Sub-therapeutic: 45.20%
  - Therapeutic: 38.40%
  - Above therapeutic level: 16.40%
- Atrial Fibrillation:
  - Sub-therapeutic: 35.20%
  - Therapeutic: 33%
  - Above therapeutic level: 31.80%
- High-risk Mitral Stenosis:
  - Sub-therapeutic: 43.60%
  - Therapeutic: 30.80%
  - Above therapeutic level: 25.60%
Pattern and route of administration of secondary prophylaxis in different income groups

- **On prophylaxis**
  - Low income countries: 69.79%
  - Lower middle income countries: 59.74%
  - Upper middle income countries: 29.25%

- **Intramuscular penicillin**
  - Low income countries: 99.1%
  - Lower middle income countries: 97.2%
  - Upper middle income countries: 45.6%

- **Oral penicillin**
  - Low income countries: 54.4%
  - Lower middle income countries: 2.82%
  - Upper middle income countries: 0.9%

*Significance levels: p=0.0012, p=0.04, p=0.0002*
• Severely affected /post-surgical patients should be on lifelong penicillin.

• We should discuss warfarin management /INR awareness and regular monitoring for patients on OACs.

• We need to consider RHD patients for novel research in new medications, innovations and interventions.
Severity of valve lesions: Native valves

<table>
<thead>
<tr>
<th>Severity of valve lesions</th>
<th>MR</th>
<th>MS</th>
<th>AR</th>
<th>AS</th>
<th>TR</th>
<th>TS</th>
<th>PR</th>
<th>PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>777</td>
<td>609</td>
<td>744</td>
<td>704</td>
<td>284</td>
<td>337</td>
<td>388</td>
<td>72</td>
</tr>
<tr>
<td>Moderate</td>
<td>744</td>
<td>625</td>
<td>704</td>
<td>123</td>
<td>264</td>
<td>388</td>
<td>264</td>
<td>78</td>
</tr>
<tr>
<td>Severe</td>
<td>704</td>
<td>725</td>
<td>284</td>
<td>78</td>
<td>388</td>
<td>123</td>
<td>321</td>
<td>72</td>
</tr>
</tbody>
</table>

Count

Severity of valve lesions

Mild: 777, 609, 744
Moderate: 704, 625, 704
Severe: 123, 264, 321
Utilisation of surgical and percutaneous interventions

- Valvuloplasty: 1% (Low income countries) vs. 4% (Low middle income countries), p=0.0042
- Surgery: 8% (Low income countries) vs. 61% (Low middle income countries), p=0.0306

*n=1109, 1351, 862  ** n=1110, 1360, 863
Surgery in total group

- **21%** Yes
- **79%** No

Income categories:
- Low income: 72.8% Replacement, 27.2% Repair
- Low middle income: 78.9% Replacement, 21.2% Repair
- Middle income: 85.5% Replacement

Low income: 72.8% Replacement, 27.2% Repair
Low middle income: 78.9% Replacement, 21.2% Repair
Middle income: 85.5% Replacement

Percentage

- Repair
- Replacement
REMEDY
Surgery: too little, too late.

The challenges of cardiac surgery for African children

ANA OH MOCUMBI

Patients awaiting surgery

LVEDD > 55

LVEDD > 55
33%

LVEDD < 55
67%

Single Valve
20%

Two Valves
44%

Three Valves
33%

Quadrivalvar disease
3%

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• Patients should be referred for intervention, particularly surgery timeously.

• This should include evidenced-based surgical procedures such as repair vs. replacement.
Access to cardiac surgery in sub-Saharan Africa

Mariana Mirabel, Antonio Grimaldi, Juergen Freers, Xavier Jouven, Eloi Marijon

DOI: http://dx.doi.org/10.1016/S0140-6736(15)60235-5

Rheumatic heart disease remains a major public health issue in developing countries.¹ Last year, Zühlke and colleagues reported the results of the first multicentre, international, hospital-based register for rheumatic heart disease.² Their study was done in tertiary centres across 12 sub-Saharan African countries, India, and Yemen, mainly including patients at an advanced stage of the disease. However, only a few patients were offered either percutaneous or surgical procedures in low-income countries, where only 11% of patients were operated on.²
Perspectives

The case for global investment in rheumatic heart-disease control
Rosemary Wyber, Liesl Zühlke & Jonathan Carapeti
Costs

- RHD exacts the highest number of disability-adjusted life-years of all cardiovascular diseases
  - 10–14-year-olds (516·6 per 100 000 people, 95% CI 425·3–647·0)
  - 5–9 years (362·0 per 100 000 people, 294·6–462·0)
- Quality of life, schooling, potential economic and emotional impact.
- US$ 791 Million-2.37 Billion in 2010
• We should consider decentralised services, consider task-sharing and involve all cadres of health care workers.

• All findings reflect health system inadequacies that perpetuate the poor access to health care experience by patients in LIMCs.
African Union Directive to Health Ministries:

- Prospective registers at sentinel sites
- Universal access to reproductive health services for women
- Decentralise technical expertise
- Adequate supplies of high-quality BPG
- Establish Centres of Excellence for cardiac surgery
- Multi-sectoral national RHD control programmes
- Cultivate strong collaborative frameworks
• Conclusions:
  • REMEDY has significant clinical and policy implications.
  • It is imperative that we act on these clear directives.
  • Key is empowering and including the patient while exercising evidence-based principles in management.
  • RHD-care should be patient-centred and health system strengthening focused.
The patient at the heart of the matter.
I would like to acknowledge all those at the 2006, 2014 and 2015 All-Africa meetings, for their vision, dedication and commitment, in particular Prof Bongani Mayosi, Dr Mark Engel and the Cape Town ASAP team.

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• Investigators and staff

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