Rheumatic Heart Disease Revisited: Patterns of Valvular Involvement from a Consecutive Cohort in Eastern Nepal

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Background

- There has been a decline in the incidence of rheumatic heart disease (RHD) in industrialized nations.
- The burden of RHD in poor and developing countries has remained a major contributor to the morbidity and premature death in the working age population.
- RHD is estimated to affect at least 15.6 million people worldwide and causes 233,000 deaths each year.

We investigated patterns of valvular involvement in patients with RHD as observed in a large tertiary care hospital in eastern Nepal.
Methods

- We retrospectively reviewed transthoracic echocardiography reports from patients diagnosed with RHD between June 1999 and February 2011.
- Echocardiographic studies were performed with Hewlett Packard Sonos 1500 using a 5 MHz transducer.
- All patients underwent a standard echocardiographic examination, including M-mode, two-dimensional and Doppler echocardiography.
B.P. Koirala Institute of Health Sciences (BPKIHS) is a university hospital in Dharan, eastern Nepal, established in 1993.

The hospital has 750 beds.

The town of Dharan has a population of 1.2 million, and the hospital is the only referral centre outside Kathmandu for the inhabitants in eastern Nepal, and also serves parts of the neighbouring states of West Bengal and Bihar in India.
BPKIHS
Results

- 10,860 transthoracic echocardiography studies performed between June 1999 and February 2011
- Diagnosis of RHD was made in 1713 patients (15.8%)
- 1055 females and 658 males were diagnosed to have RHD (gender ratio 1.6:1)
- 25.7% of the patients being <20 years of age
Figure 1. Distribution of Age and Gender Among Patients Presenting with RHD

| Age Group     | Women | Men | N (%)
|---------------|-------|-----|------
| Overall       | 1055  | 658 | 1713
| <20 years     | 205   | 236 | 441 (25.7)
| 20-29 years   | 300   | 156 | 456 (26.6)
| 30-39 years   | 188   | 110 | 298 (17.4)
| 40-49 years   | 194   | 72  | 266 (15.5)
| ≥50 years     | 168   | 84  | 252 (14.7)

p < 0.001
Mitral regurgitation (MR) was the most common valvular lesion across all age groups irrespective of gender (n=1321, 77.1% {isolated and combined}).

Female patients were significantly older as compared to male patients at the time of presentation (32.8±15.2 years versus 28.5±15.4 years, p<0.001)
- Mitral stenosis was more common in females (62.8% versus 51.5%, p<0.001)
- Conversely, aortic regurgitation (AR) was more common in males as compared to females (55.6% versus 48.9%, p=0.007)
- Involvement of both the mitral and the aortic valve was observed in 49.8% of the patients and was more common in males as compared to females (52.7% versus 47.8%, p=0.047)
- A combination of MR with MS (19.3%) or with AR (17.9%) were the most common finding.
- Echocardiographic evidence of infective endocarditis was documented in 212 (12.4%) patients
- Pulmonary hypertension was observed in 34.9% of our cohort.
Figure 2. Numbers and Percentages of Left-sided Valvular Involvement

Valvular Pathology | Percentage of Total |
--- | --- |
MS | 10.3% |
MR | 15.9% |
AS | 0.2% |
AR | 3.2% |
MS+MR | 19.3% |
AS+AR | 1.3% |
MR+AR | 17.9% |
MS+AS | 0.8% |
MR+AS | 0.5% |
MS+AR | 5.4% |
MS+MR+AR | 15.7% |
MS+MR+AS | 1.3% |
MR+AR+AS | 2.2% |
MS+AS+AR | 1.9% |
MS+MR+AS+AR | 4.0% |

Single-Valve Involvement 50.3%
Combined Valvular Involvement 49.7%

MS = Mitral Stenosis; MR = Mitral Regurgitation; AS = Aortic Stenosis; AR = Aortic Regurgitation
Figure 3. Patterns of Valvular Involvement Stratified by Age Groups

- Mitral Regurgitation: 77.1%
- Mitral Stenosis: 58.5%
- Aortic Regurgitation: 51.5%
- Aortic Stenosis: 12.3%

<table>
<thead>
<tr>
<th>Age Group</th>
<th>N (%)</th>
<th>Mitral Regurgitation</th>
<th>Mitral Stenosis</th>
<th>Aortic Regurgitation</th>
<th>Aortic Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 years</td>
<td>441 (25.7)</td>
<td>83.7</td>
<td>54</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>20-29 years</td>
<td>456 (26.6)</td>
<td>77.9</td>
<td>60.3</td>
<td>12.1</td>
<td>12.1</td>
</tr>
<tr>
<td>30-39 years</td>
<td>298 (17.4)</td>
<td>72.5</td>
<td>68.1</td>
<td>12.1</td>
<td>12.1</td>
</tr>
<tr>
<td>40-49 years</td>
<td>266 (15.5)</td>
<td>70.3</td>
<td>69.5</td>
<td>17.7</td>
<td>17.7</td>
</tr>
<tr>
<td>≥50 years</td>
<td>252 (14.7)</td>
<td>77</td>
<td>55.2</td>
<td>54.4</td>
<td>54.4</td>
</tr>
</tbody>
</table>

(p values: Mitral Regurgitation vs Mitral Stenosis: p<0.001; Mitral Regurgitation vs Aortic Regurgitation: p<0.015; Mitral Regurgitation vs Aortic Stenosis: p<0.001)
Conclusions

- (1) The prevalence of RHD among patients referred for transthoracic echocardiography in this single-center experience from eastern Nepal was high.
- (2) One in four patients diagnosed with RHD was younger than 20 years of age.
- (3) More than 60% of the patients diagnosed with RHD were females.
- (4) Differential patterns of valvular involvement were observed across gender and age categories.
A combination of poverty, lack of awareness, limited access to primary prevention and secondary prophylaxis entertain ARF and make RHD an unresolved problem in this part of the world.

Once significant valvular disease has developed medical options are limited; cardiac surgery for valve replacement is available in the capital city of Kathmandu 500 kilometers west of Dharan and percutaneous mitral valvotomy has only recently been introduced in our centre.
Limitations

- The analyzed cohort reflects a selected patient population that was referred for echocardiography. The reasons for referral to echocardiography and symptom status have not been documented in the echocardiography database and could not be assessed retrospectively.

- No longitudinal follow-up was performed; hence echocardiographic findings could not be correlated with clinical outcome.

- This analysis reflects a single centre, hospital based retrospective observation.
What we intend to do?
A Population-Based Study of Prevalence of Rheumatic Heart Disease and Cardiovascular Outcomes among Schoolchildren in Nepal

ClinicalTrials.gov Identifier: NCT01550068

Nikesh R Shrestha (Nepal), Thomas Pilgrim (Switzerland), Bindu Kalesan (Switzerland), Prahlad Karki (Nepal), Anil Basnet (Nepal), Bernhard Meier (Switzerland), Philip Urban (Switzerland)

Funded by the La Tour Foundation, Geneva, Switzerland
Phase 1

- a cross-sectional survey of schoolchildren between the ages of 5-15 years from public and private schools in urban and rural areas in Southeast Nepal will be performed, applying the World Heart Federation criteria for echocardiographic diagnosis of RHD. (auscultation and echo)

Phase 2

- Using the results of the survey, those children with documented history of acute rheumatic fever and/or echocardiographic evidence of RHD will be enrolled in a prospective cohort study.
Map showing reported worldwide prevalence of RHD from 1991 through present. (From: Seckeler MD, Hoke TR. The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. Clinical Epidemiology 2011;3:67-84.)
Seventeen publications qualified for inclusion into the meta-analysis, and examined between 362 and 229,829 schoolchildren either by
- primary cardiac auscultation followed by selective echocardiography
- or in combination with echocardiography
Meta-Analysis of Prevalence of Rheumatic Heart Disease Using Cardiac Auscultation

### Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Auscultation</th>
<th>Prevalence rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South-east Asia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bahadur KC</td>
<td>11/9420</td>
<td>1.17 (0.48, 1.86)</td>
</tr>
<tr>
<td>Jose VJ</td>
<td>157/229829</td>
<td>0.68 (0.58, 0.79)</td>
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<tr>
<td>Periwal KL</td>
<td>50/3002</td>
<td>16.66 (12.08, 21.23)</td>
</tr>
<tr>
<td>Marijon E</td>
<td>8/3677</td>
<td>2.18 (0.67, 3.68)</td>
</tr>
<tr>
<td>Bhaya M</td>
<td>1/1059</td>
<td>0.94 (-0.91, 2.79)</td>
</tr>
<tr>
<td>Saxena A</td>
<td>5/6270</td>
<td>0.80 (0.10, 1.50)</td>
</tr>
<tr>
<td>Sadiq M</td>
<td>546/24980</td>
<td>21.86 (20.04, 23.67)</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td>5.85 (2.93, 8.78)</td>
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<table>
<thead>
<tr>
<th>Central America</th>
<th></th>
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<tbody>
<tr>
<td>Nordet P</td>
<td>6/25519</td>
<td>0.24 (0.05, 0.42)</td>
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<tr>
<td><strong>Subtotal</strong></td>
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<td>0.24 (0.05, 0.42)</td>
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<table>
<thead>
<tr>
<th>Africa</th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijon E</td>
<td>5/2170</td>
<td>2.30 (0.29, 4.32)</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td>2.30 (0.29, 4.32)</td>
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<table>
<thead>
<tr>
<th><strong>Overall</strong></th>
<th></th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>4.05 (2.80, 5.30)</td>
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</table>
# Meta-Analysis of Prevalence of Rheumatic Heart Disease Using Echocardiography

## Study by Region

<table>
<thead>
<tr>
<th>Study</th>
<th>Echocardiography</th>
<th>Prevalence rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>South-east Asia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijon E</td>
<td>79/3677</td>
<td>21.48 (16.80, 26.17)</td>
</tr>
<tr>
<td>Bhaya M</td>
<td>54/1059</td>
<td>50.99 (37.74, 64.24)</td>
</tr>
<tr>
<td>Saxena A</td>
<td>128/6270</td>
<td>20.41 (16.91, 23.91)</td>
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<tr>
<td><strong>Subtotal (I-squared = 89.6%, p&lt;0.0001)</strong></td>
<td></td>
<td>28.17 (17.96, 38.39)</td>
</tr>
<tr>
<td><strong>Central America</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paar JA</td>
<td>150/3150</td>
<td>47.62 (40.18, 55.06)</td>
</tr>
<tr>
<td><strong>Subtotal (I-squared = .%, p = .)</strong></td>
<td></td>
<td>47.62 (40.18, 55.06)</td>
</tr>
<tr>
<td><strong>Africa</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijon E</td>
<td>66/2170</td>
<td>30.41 (23.19, 37.64)</td>
</tr>
<tr>
<td><strong>Subtotal (I-squared = .%, p = .)</strong></td>
<td></td>
<td>30.41 (23.19, 37.64)</td>
</tr>
<tr>
<td><strong>Overall (I-squared = 93.4%, p&lt;0.0001)</strong></td>
<td></td>
<td>33.18 (22.64, 43.71)</td>
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</tbody>
</table>
Recorded prevalence rates for RHD among schoolchildren in Southeast Asia amounted to

- 5.9 (95% CI 2.9 to 8.8) as assessed by cardiac auscultation
- 28.2 (95% CI 18.0-38.4) as assessed by echocardiography

suggesting a five-fold increased detection rate by echocardiography
We performed a pilot study in February 2012.
The results of a pilot study (N=54) performed in one private school in urban Southeast Nepal identified two children to have borderline RHD (prevalence rate=37 per 1000).
Thank you