Cascade FH Registry

CONDITION: Familial Hypercholesterolemia (FH), a genetic condition marked by dramatically high levels of LDL-C that are not related to diet or lifestyle.

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CONTACT INFO: Christine Majeski, RN | christine.majeski@allina.com | 612-863-3546

DESCRIPTION: A national registry tracking the longitudinal treatment, clinical outcomes and patient reported outcomes of FH with the aim of increasing awareness and family screening of FH.

CRITERIA LIST/ QUALIFICATIONS:

**Inclusion:**
- Patient with existing diagnosis of FH using one of the three diagnostic tools:
  - US MedPed Program Criteria
  - Simon Broome Register Criteria with a diagnosis of “probable”
  - Dutch Lipid Clinic Network Diagnostic Criteria with a diagnosis of “probable”
- Patients with FH genetic mutation

**Exclusion:**
- Patients with a known medical condition other than FH thought to contribute to hyperlipidemia (i.e. untreated hyperthyroidism, nephrotic syndrome, cholestasis hypopituitarism)

SPONSOR: FH Foundation
Cardiovascular disease trends in Developing Countries

Moses K. Wananu, MD
Cardiology Fellow.
Minneapolis Heart Institute/ Hennepin County Medical Center.

Objectives

- Disease trends in developing countries over the decades.
- Pattern of Cardiovascular diseases in African countries.
- Treatment and limitation.
- risk factors.
- Way forward.
- Personal project.
- Take home points.
Disease trends.

- Meta analysis of 27 studies reporting 86,307 medical admissions from 1950-2010
- The diseases reported were grouped into body systems according to International Classification of diseases (ICD) guidelines.
- Infectious and parasitic, Respiratory, Circulatory, digestive, nervous, endocrine, Genitourinary and others.

Hospital admissions over the decades
Systemic review of medical admissions in Adults – African countries

- Infectious and parasitic diseases were the leading cause of admission 19.8% over the period.
- Respiratory illness was second accounting for 16.2%
- Circulatory system third with 11.3%
- NOTE: Proportion of admission due to circulatory system disorder increased 5x (3.9% in 1950-59 to 19.9% in 2000-2010) RR 5.1, x2 test for trend p<0.00005.

Systemic review of medical admissions in Adults – African countries

- Infectious and parasitic diseases decreased from 18.2% to 13.9% of all admissions over the period. 24% decrease (RR 0.76, 95% CI 0.71-0.82)
- Respiratory decreased from 16.2% to 7.7% of all admissions.
- Endocrine and nervous system disorders increased significantly over the period for each account for <5% of all admissions.
Systemic review of In Hospital Deaths of Adults in African countries

Death from infectious and parasitic diseases rose from 11.8 in 1950-59 to 19.2 in 2000-2010. HIV likely explanation.

Summary:
- Per WHO predicts that by 2020, the causes of diseases and death in SSA will have undergone a significant shift towards endemic non-communicable diseases and away from infectious diseases.
WHO TOP TEN LEADING CAUSES OF DEATH GLOBALLY

- Ischaemic heart disease
- Stroke
- Lower respiratory diseases
- Diarrhoeal diseases
- Tuberculosis
- HIV/AIDS
- Maternal causes
- Tuberculosis
- Malaria
- Road injuries

WHO TOP TEN LEADING CAUSES OF DEATH GLOBALLY

- Ischaemic heart disease
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- Tuberculosis
- HIV/AIDS
- Maternal causes
- Tuberculosis
- Malaria
- Road injuries
WHO TOP TEN LEADING CAUSES OF DEATH

<table>
<thead>
<tr>
<th>Middle-income countries</th>
<th>Deaths in millions</th>
<th>% of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>5.27</td>
<td>13.7%</td>
</tr>
<tr>
<td>Stroke and other cerebrovascular disease</td>
<td>4.91</td>
<td>12.8%</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>2.79</td>
<td>7.2%</td>
</tr>
<tr>
<td>Lower respiratory infections</td>
<td>2.07</td>
<td>5.4%</td>
</tr>
<tr>
<td>Diarrhoeal diseases</td>
<td>1.68</td>
<td>4.4%</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1.03</td>
<td>2.7%</td>
</tr>
<tr>
<td>Road traffic accidents</td>
<td>0.94</td>
<td>2.4%</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0.93</td>
<td>2.4%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.87</td>
<td>2.3%</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>0.83</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

WHO TOP TEN LEADING CAUSES OF DEATH
WHO TOP TEN LEADING CAUSES OF DEATH

The top 10 causes of death in lower-middle-income economies 2015

- Ischaemic heart disease
- Stroke
- Lower respiratory infections
- Diarrhoeal disease
- Chronic obstructive pulmonary disease
- Tuberculosis
- Lower intestinal infections
- Diabetes mellitus
- Pneumonia
- Road injury

Deaths per 100,000 population

4 stages of epidemiologic transition

<table>
<thead>
<tr>
<th>The Epidemiologic Transition</th>
<th>Life Expectancy</th>
<th>% deaths from CV</th>
<th>Dominant CVDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 Prevalence and Family</td>
<td>35 years</td>
<td>&lt;10</td>
<td>Infectious (RHD) Multifocal</td>
</tr>
<tr>
<td>Stage 2 Receding pandemics</td>
<td>50 years</td>
<td>10.35</td>
<td>Infectious (RHD) Stroke-neurologic</td>
</tr>
<tr>
<td>Stage 3 Degenerative and non-acute diseases</td>
<td>&gt;60 years</td>
<td>38.65</td>
<td>Ischaemic heart disease (HD) Stroke – haemorrhagic, ischaemic</td>
</tr>
<tr>
<td>Stage 4 Delayed degenerative diseases</td>
<td>&gt;70 years</td>
<td>40-50</td>
<td>HD Stroke – ischaemic CHF</td>
</tr>
</tbody>
</table>
Stages of health, nutrition and demographic change.

Trend of NCDs over the decades
Noncommunicable diseases.

Causation pathway of non-communicable disease

Adapted from: The Lancet (2011) 377: 899-909
Early vs Late intervention impact

Objectives

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- Treatment and limitation
- Risk factors.
- Way forward
- Take home points.
Pattern of myocardial infarction in African countries

**Figure 1.** Age and gender distribution of acute myocardial infarction.
Comparing MI: African vs Western countries.

**Table 3. – Mean age of myocardial infarction reported from various populations**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Countries</th>
<th>Mean age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abubakar et al. 2004</td>
<td>England</td>
<td>69.3</td>
</tr>
<tr>
<td>Otter et al. 2007</td>
<td>Germany</td>
<td>68</td>
</tr>
<tr>
<td>Seyoum and Leake, 2010</td>
<td>Eritrea</td>
<td>59.8</td>
</tr>
<tr>
<td>Mamo and Oli, 2001</td>
<td>Ethiopian</td>
<td>55.1</td>
</tr>
<tr>
<td>Seck et al., 2007</td>
<td>Senegal</td>
<td>59.0</td>
</tr>
<tr>
<td>Current study</td>
<td>Kenya</td>
<td>56.8</td>
</tr>
</tbody>
</table>

Pattern of myocardial infarction in African countries

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Country</th>
<th>Population</th>
<th>Subjects with MI (n)</th>
<th>Total Subjects (n)</th>
<th>Prevalence of MI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adebisi et al (2003/17)</td>
<td>South Africa</td>
<td>Patients admitted for acute stroke</td>
<td>4</td>
<td>555</td>
<td>0.7%</td>
</tr>
<tr>
<td>Ahmed, et al (2002/18)</td>
<td>Sudan</td>
<td>Diabetic patients who died while in hospital</td>
<td>7</td>
<td>67</td>
<td>10.4%</td>
</tr>
<tr>
<td>Sark, et al (2000/19)</td>
<td>Nigeria</td>
<td>Inpatients on medical ward</td>
<td>22</td>
<td>3124</td>
<td>0.7%</td>
</tr>
<tr>
<td>Seck, et al (2002/20)</td>
<td>Senegal</td>
<td>Emergency department patients</td>
<td>32</td>
<td>174,429</td>
<td>0.1%</td>
</tr>
<tr>
<td>Obi, et al (2010/16)</td>
<td>Nigeria</td>
<td>Inpatients on medical ward</td>
<td>14</td>
<td>6647</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

doi:10.1271/biolonomy.0956880X02
Mortality.

Table 5. – Mortality rates in AMI cases reported from sub-Saharan African countries

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seck et al., 2007¹⁹</td>
<td>Senegal</td>
<td>21</td>
</tr>
<tr>
<td>Seyoum and Leake, 2010⁵</td>
<td>Eritrea</td>
<td>35.8</td>
</tr>
<tr>
<td>Fikreyesus and Bahia, 1989¹³</td>
<td>Ethiopia</td>
<td>29.4</td>
</tr>
<tr>
<td>Selfel and Kew, 1970¹⁷</td>
<td>South Africa</td>
<td>33</td>
</tr>
<tr>
<td>Bertrand, 1992²⁹</td>
<td>Ivory Coast</td>
<td>15</td>
</tr>
<tr>
<td>Arjorin et al., 2005¹²</td>
<td>Nigeria</td>
<td>39</td>
</tr>
<tr>
<td>Current study, 2010</td>
<td>Kenya</td>
<td>5</td>
</tr>
</tbody>
</table>

Death attributable to CVD
MI presentation and diagnosis

- **Presentation**
  - Chest pain and tightness (75.8%)
  - Fainting (9.2%)
  - Dizziness (6.7%)
  - Nausea and vomiting (4.9%)
  - Diaphoresis and extreme weakness (3.3%)

- **Diagnosis**
  - ST deviation AND CK-mb and Trop (87.5%)
  - Angiography (8.3%) or Echocardiogram (4.2%)

Objectives

- Disease trends in developing countries over the decades.
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- **Treatment and limitation.**
  - risk factors.
  - Way forward.
  - Personal project.
  - Take home points.
Treatment

- All patients: Oxygen, Sublingual nitroglycerine, Aspirin, beta blockers and ACEI within 6 hrs.
- STEMI started on thrombolytic and heparin treatment within 12 hrs. (35% no improvement on this regiment)
- 20% offered to be taken for angioplasty if no improvement.
- 10% of ones who undergo angioplasty referred for CABG within or abroad.

Limitations

- 50% recover completely without complications within 4 weeks.
- 44% develop cardiac failure.
- 5% die.
- Major limitation:
  - Resources,
  - no clear guidelines on how to approach a patient p/w sx suspicious for AMI,
  - Extremely poor follow up (patient education lacking).
Publications per year/ countries.

Publication trends by topics

<table>
<thead>
<tr>
<th>Table 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of articles indexed in MEDLINE by Sub-Saharan African (SSA) authors in top-ten producing nations on the five most common SSA diseases published between 1995 and 2004</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Region</th>
<th>HIV/AIDS</th>
<th>Malaria</th>
<th>Parasitic disease</th>
<th>Cancer</th>
<th>Cardiovascular disease</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>South</td>
<td>799</td>
<td>7%</td>
<td>89%</td>
<td>1%</td>
<td>1051%</td>
<td>12,193</td>
</tr>
<tr>
<td>Africa</td>
<td>149</td>
<td>3%</td>
<td>208%</td>
<td>4%</td>
<td>362%</td>
<td>4,727</td>
</tr>
<tr>
<td>Nigeria</td>
<td>163</td>
<td>8%</td>
<td>235%</td>
<td>12%</td>
<td>95%</td>
<td>1,587</td>
</tr>
<tr>
<td>Kenya</td>
<td>150</td>
<td>15%</td>
<td>32%</td>
<td>3%</td>
<td>85%</td>
<td>989</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>43</td>
<td>4%</td>
<td>121%</td>
<td>12%</td>
<td>83%</td>
<td>981</td>
</tr>
<tr>
<td>Senegal</td>
<td>103</td>
<td>12%</td>
<td>29%</td>
<td>3%</td>
<td>49%</td>
<td>885</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>114</td>
<td>16%</td>
<td>85%</td>
<td>12%</td>
<td>33%</td>
<td>719</td>
</tr>
<tr>
<td>Ghana</td>
<td>34</td>
<td>5%</td>
<td>67%</td>
<td>10%</td>
<td>22%</td>
<td>670</td>
</tr>
<tr>
<td>Uganda</td>
<td>193</td>
<td>29%</td>
<td>62%</td>
<td>9%</td>
<td>39%</td>
<td>664</td>
</tr>
<tr>
<td>Cameroon</td>
<td>35</td>
<td>5%</td>
<td>100%</td>
<td>15%</td>
<td>37%</td>
<td>660</td>
</tr>
<tr>
<td>Total</td>
<td>1,753</td>
<td>7%</td>
<td>1,023%</td>
<td>4%</td>
<td>1,836%</td>
<td>24,415</td>
</tr>
</tbody>
</table>
Objectives

☐ Disease trends in developing countries over the decades.
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☐ Treatment and limitation.
☐ **Risk factors.**
☐ Way forward.
☐ Personal project.
☐ Take home points.

---

Risk Factors

<table>
<thead>
<tr>
<th>Population</th>
<th>Predominant risk factors in order of prominence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa Review</td>
<td>Hypertension, smoking, diabetes, abdominal obesity, dyslipidaemia</td>
</tr>
<tr>
<td>INTERHEART Africa study</td>
<td>Smoking, diabetes, hypertension, abdominal obesity, dyslipidaemia</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Hypercholesterolaemia, hypertension</td>
</tr>
<tr>
<td>Senegal</td>
<td>Hypertension, smoking, diabetes</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Hypertension, diabetes mellitus, smoking, hyperlipidaemia</td>
</tr>
<tr>
<td>Black South Africa</td>
<td>Hypertension, dyslipidaemia, diabetes</td>
</tr>
<tr>
<td>Kenya</td>
<td>Hypertension, diabetes, smoking and infection</td>
</tr>
</tbody>
</table>
Risk Factors

Table 1. – Frequency of risk factors for myocardial infarction

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Frequency</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>42</td>
<td>(35)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>25</td>
<td>(20.8)</td>
</tr>
<tr>
<td>Smoking</td>
<td>15</td>
<td>(12.5)</td>
</tr>
<tr>
<td>Infections</td>
<td>15</td>
<td>(12.5)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>4</td>
<td>(3.3)</td>
</tr>
<tr>
<td>Obesity</td>
<td>4</td>
<td>(3.3)</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>4</td>
<td>(3.4)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>2</td>
<td>(1.7)</td>
</tr>
<tr>
<td>Multiple factors</td>
<td>9</td>
<td>(7.5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>120</strong></td>
<td><strong>(100)</strong></td>
</tr>
</tbody>
</table>

Risk Factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Deaths ($\times 10^3$)</th>
<th>% of total death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>7141</td>
<td>12.8</td>
</tr>
<tr>
<td>Tobacco</td>
<td>4907</td>
<td>08.8</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>4415</td>
<td>07.9</td>
</tr>
<tr>
<td>Low fruit &amp; veg</td>
<td>2726</td>
<td>04.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>2591</td>
<td>04.6</td>
</tr>
<tr>
<td>Alcohol</td>
<td>1804</td>
<td>03.2</td>
</tr>
<tr>
<td>Phys. inactivity</td>
<td>1922</td>
<td>03.4</td>
</tr>
</tbody>
</table>
Diabetes

Prevalence of metabolic syndrome among urban population in Kenya

- Tg > 150 mg/dl, HDL < 40 mg/dl (males) and < 50 mg/dl (females), BP > 130/85, Waist circ. Males > 38 in, females > 35 in, FPG > 100 mg/dl
- 32% of population living in urban areas
- Prevalence 34.6% higher in women than men (40.2 vs 29% respectively). Lydia et al.
- Overweight 39.8 vs 15.8 and obesity 15.5 vs 5.1% among urban vs rural Kenyan population respectively. Christiansen et al.

Prevalence of metabolic syndrome among urban population in Kenya

- HTN, low HDL, Central Obesity most common.
- Social economic status emerged as a significant factor for developing metabolic syndrome in men but not in women.
- Higher level of education was a significant factor (protective) in women than men.
- Increasing age. Prevalence increases from ages 35 with the most affected group being >55.

NCD effect on development

- Early death affecting most productive age groups. (causing negative impact on productivity and development.
- Cause poverty: Expensive treatment for NCD. Buying products such as tobacco, unhealthy diet making population prone to NCD.
- Burden of NCD predicted to impede poverty reduction initiatives.
- Threatening to compromise development gains.
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Personal project

- 2011 helped organize first mission trip to Africa for Hearts around the world – Kenya.
- 28 patients diagnosed with CAD were selected after screening approximately 100 charts of patients in hospital, and performing 40 echocardiograms.
- 3 open heart surgeries were done for Valve disease and 1 CABG. The rest PCI with or without stenting.
challenges

- Largest Hospital did not have a functioning Cardiac Catheterization laboratory.
- Cost – CABG w/wo AVR Ksh600-800,000 = $7,317 - 9756. Average annual house hold income $976-$1800.
- PCI – Ksh200,000-300,000 = $2439-3658
- Pt buys heart valve – for $100 dollars donated, expired. Same goes for stents, pacemaker etc – has now shifted.

challenges

- Outcome – Mortality s/p Open heart surgery 15%
- “multispecialized surgeons”- heart surgeon does adult, pediatric, renal transplant.
- 10-20 cardiologist in the country at that time. Pop > 40,000,000
- Medical tourism to India
- Poor follow up after surgery leading to high complication rates.
- Mistrust to western volunteer organization – “hostile takeover” – described by a cardiologist.
challenges

KNH during open heart surgery.

Trip accomplishment

- Did CT surgery for Ksh100,000 = $1,219
- PCI for Ksh30,000 = $365.
- Mode of operation.
  - Actively assisting (sonographer, surgeon, interventionalist, cardiologist, perfusionist, ICU rounding after surgery, Nursing)
- In first few hours had cases for the week. (quality vs quantity in training)
Current Status

- Cathlab has been rebuild and is operational.
- CT surgery is still very expensive.
- However PCI is now $175 dollars.
- Collaboration of African teaching hospitals with international universities to conduct quality studies.
- Over half the country is now insured making it easier to pay for procedures.

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Conclusion

- There is rapidly increasing cardiovascular risk factors as a result of adverse behavioral and epidemiological transition.
- In some districts CVD is leading cause of death.
- Risk factors are similar to other developed countries with exception of infectious diseases

Conclusion

- There is an urgent need to prepare and focus resources to address what is expected to be the leading cause of death by 2030 in a lot of developing SSH countries.
- More quality studies need to be done to better understand intervention and outcomes.
- The approach of “teaching a fisherman how to fish” through collaborations with international teaching hospitals and organizations are likely to make considerable impact and is better received.
THANK YOU!

Questions?