Worldwide Variations in the Epidemiology of Infective Endocarditis: A View from the Middle East

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  - Astra-Zeneca
Middle East and North Africa Region (MENA): FACTS!

- Population: 355 million
- No. of countries: 19
- Population distribution:
  - 85% in middle-income countries
  - 8% in high-income countries
  - 7% in low-income countries

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Endocarditis in the MENA Region

- Single center case-series
- Case reports
- No national or global epidemiological studies
- No population-based studies

- Variability in access to care, diagnostic methods (mainly TEE), antibiotic therapy, and surgical intervention
- Variability in quality of care

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## Endocarditis in the MENA Region: No. of Hits on PubMed

<table>
<thead>
<tr>
<th>Country</th>
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<td>Saudi Arabia</td>
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<td>Turkey</td>
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</table>

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Epidemiology of IE in MENA

- Retrospective analysis of IE from 1995 to 2008
- 54 cases of definite endocarditis (male to female ratio 2.6:1)
- Mean age 59.7 ± 18.2 years
- Microbiology:
  - *S. aureus* (n = 23)
  - *Enterococcus faecalis* (n = 12)
  - Viridans streptococci (n = 9)
- In-hospital mortality 29.4%
Epidemiology of IE in MENA

- Tertiary hospital in Riyadh, Saudi Arabia
- Retrospective review between 1993-2003
- N = 47 patients (37 NVE, 10 PVE)
- Predisposing cardiac conditions in 27 patients (RHD, CHD)
- Microbiology:
  - Staphylococci (n = 20); 12 S. aureus, 8 CoNS
  - Enterococci (n = 6)
- In-hospital mortality rate: 8.5%

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Epidemiology of IE in MENA

- Nosocomial infective endocarditis (NIE) is increasingly described
- 3 cases of NIE at a tertiary care hospital over 2 years
  - Burn patient
  - Liver transplant recipient
  - Renal transplant recipient
- All had indications for surgery but was only performed in 2:
  - Burn patient → underwent surgery → survived
  - Liver transplant recipient → poor surgical candidate → died
  - Renal transplant recipient → underwent surgery → died post-op

Haddad SH. Int J Infect Dis 2004;8:210-6

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Epidemiology of IE in MENA

- Multicenter retrospective study in Tunisia from 1991 to 2000
- 440 IE in 435 patients (242 males, 193 females)
- Mean age 32.4 (range 1-78) years
- RHD most common predisposing heart disease (45.2%)
- Blood cultures negative in 53.6%
- Microbiology:
  - Staphylococci (17.9%)
  - Streptococci (17.3%)
  - Enterococci (3.9%)
- Early valve surgery performed in 51.2% of patients
- In-hospital mortality 20.6%

Epidemiology of IE in MENA

- High-volume tertiary care center in Tunisia
- 134 patients with endocarditis between 1997 and 2006
- Mean age 34.22 years.
- RHD predominant underlying heart condition (45%).
- In 66 cases (49%), blood cultures were negative
- Microbiology:
  - Staphylococci (N = 30); 24 S. aureus, 6 CoNS
  - Streptococci (N = 32)
- Overall mortality 19%; predictors:
  - CHF (HR = 5.34, 95% CI 1.67-17.15, p = 0.005)
  - Vegetations >15 mm (HR = 5.78, 95% CI 1.84-18.32, p = 0.002)
Epidemiology of IE in MENA

- To study the effect of type of treatment on outcome of PVE in a tertiary care center in Tunisia between 1997 and 2006
- 48 PVE episodes (30 men and 18 women), mean age 37.93 years
  - 28 patients (58.33%) treated medically
  - 20 (41.66%) treated by a combined surgical and medical strategy
- Indications for surgery: hemodynamic deterioration (n = 8), annular abscess (n = 6), persisting sepsis (n = 6)
- Operated patients had longer delay to diagnosis, more heart failure and early complications, and more prosthetic dehiscence, annular abscesses and vegetations >10 mm
- Mortality: 14% in medical group, 35% in surgical group (p=0.09)

Rekik S. Neth Heart J 2009;17:56-60
Epidemiology of IE in MENA

- To determine the frequency, clinical features and etiological factors of culture-negative endocarditis
- Retrospective review of 98 cases of IE from 1991 to 2000 in Sousse, Tunisia
- 48 patients (48.9%) had negative blood cultures:
  - Org identified in 7 cases by other techniques
  - 41 cases cause of IE not determined
- Factors associated with negative blood cultures:
  - Higher incidence of previous antibiotic therapy
  - Extracardiac signs of IE
  - Cardiac failure
- Early surgical indications and mortality were the same in both groups
Blood culture-negative endocarditis is common in Algeria

To describe the etiology of IE in this country

77 cases of definite IE and 33 cases of possible IE

Blood cultures negative in 62 cases

- 34 cases unidentified
- 28 cases identified by other means, 18 caused by zoonotic and arthropod-borne bacteria: *Bartonella quintana* (14 cases), *Brucella melitensis* (2 cases), and *Coxiella burnetii* (2 cases)
Epidemiology of IE in MENA

- 72 patients with suspected IE in a teaching hospital in Sana’a, Yemen between 2005 and 2007
- Mean age was 28.56 ± 14.5 years; 30 men and 42 women
- RHD in 53.3% of patients
- Blood cultures positive in only 7 cases (9.6%)
- Addition of high ESR as minor criteria improved the diagnostic possibility
- In hospital mortality 12.5 %
Unusual Presentations of IE in MENA

- IE presenting as isolated splenomegaly (Iran)
  

- IE causing acquired aorto-ventricular tunnel (Iran)
  
  Moaref A. Echocardiography 2009;26:82-3

- Tricuspid valve IE in an intravenous drug abuser masquerading as pulmonary tuberculosis (Oman)
  
  Panduranga P. Heart Views 2010;11:121-4
Unusual Organisms Causing IE in MENA

- **Salmonella** species (KSA)
- **Granulicatella elegans** (KSA)
- **Kytococcus Schroeteri** (Tunisia)
- **Mycobacterium abscessus** (Kuwait)
- **Chryseomonas luteola** (Morocco)
- **Pasteurella multocida** (Lebanon)
- **Trichosporon beigeli** (Lebanon)
- **Gemella morbillorum** (Qatar)

References:

- Al-Tawfiq JA. Diagn Microbiol Infect Dis 2007;57:439
- Mnif B. J Clin Microbiol 2006;44:1187
- Chihab W. J Clin Microbiol 2004;42:1837
- Naba MR. Int J Infect Dis 2009;13:e267
- Mooty MY. Eur J Clin Microbiol Infect Dis 2001;20:139
Brucella IE in MENA

- Single reports or short series from Iran, KSA, Qatar, and Jordan
- Large series from Turkey:
  - Medical and surgical treatment are needed simultaneously
  - Perioperative antibiotic therapy combined with surgical treatment increases the quality of life in the long-term follow-up
  - Continue antibiotics for at least 6 months after surgery
  - Medical therapy alone can be an alternative in stable patients (combination of three antibiotics)

Amirghofran AA. Ann Thorac Surg 2011;92:e77
Esmailpour N. Trop Doct 2010;40:47
Al-Majid FM. Saudi Med J 2010;31:448
Alsoub H. Clin Microbiol Infect 2001;7:382
Fedakar A. Trop Doct 2011;41:227
Sasmazel A. Ann Thorac Surg 2010;89:1432
Inan MB. Clin Cardiol 2010;33:E20
Cay S. Kardiol Pol 2009;67:274

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IE in the Hemodialysis Population

- Tunisian series:
  - Mostly staphylococci (68.7%)
  - Frequent complications
  - High mortality (43.7%)

- Moroccan series:
  - Staphylococci and enterococci
  - Recent history of infected vascular access
  - Median survival after surgery: 10.3 months

IE in the Transplant Population

- Kidney transplant recipients:
  - 4 patients with IE in Iran
  - All 4 patients were treated successfully
  - Early diagnosis and medical/surgical management can preserve the patient and the kidney allograft
  - Testing for concurrent infections such as CMV is warranted

- Does CMV increase risk of IE in renal transplant?
  - Retrospective study in Iran
  - Presentation time of IE in CMV-positive patients was earlier than in CMV-negative patients

References:
- Einollahi B. Ann Transplant, 2009;14:32-37

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Surgical Treatment of IE in MENA

- Short-term and long-term outcome of surgery in Tunisia
- 88 cases of IE requiring surgery (70 NVE and 18 PVE)
- Mean age 34.9 years, 54 (61.4%) were men
- *Streptococcus* species were most common
- Most frequent indication for operation was congestive heart failure
- Early mortality: 27.27%
- 5- and 10-year survivals free from the combined endpoint of recurrent IE, cardiovascular death and late surgery in survivors were 69.5% and 63.7%, respectively
- Surgery for IE remains challenging and yields high mortality rates
- Severe heart failure is most powerful predictor of mortality
- Long-term outcome is satisfactory
Complications and Outcome of IE in MENA

- Predictors of bad prognosis of IE in a Tunisian series:
  - Vegetation > 10 mm (OR 1.97, 1-4.1, p = 0.05)
  - Presence of a neurological accident (OR: 2.76, 1.32-5.76, p = 0.007)
  - Absence of surgical treatment (OR: 5.03, 2-11.4, p < 0.001)
Complications and Outcome of IE in MENA

- Moroccan series looking at vascular complications in 12 patients with IE and 26 vascular complications:
  - 11 neurological
  - 10 arterial involving the limbs including 5 mycotic aneurysms
  - 2 acute myocardial infarcts
  - 2 splenic infarcts
  - 1 recurrent septic pulmonary embolism

- Vascular disease initial manifestation in 9 patients
- 54% occurred before end of 2nd week of antibiotic treatment
- 4 deaths; 3 directly related to the vascular complication
Awareness About IE in MENA

Parents of 205 children in several cardiology clinics in KSA were interviewed

- Patients' mean age was 5 years and 8 months (range 1 month-15 years)
- 50% of parents were high school graduates
- 25% of parents correctly defined endocarditis
- 64% of parents with at risk children were aware of measures to prevent endocarditis
- Parental knowledge of endocarditis was limited
- Intensified education and awareness programs are needed
Data from Lebanon
Endocarditis in Pediatric Age Group

41 children between 1977 and 1995
Age: 11.3 ± 2.8 y
24 female, 17 male

- viridans streptococci and S. aureus most common

46% congenital heart disease (tetralogy, pulmonic stenosis)
39% rheumatic heart disease

- Overall mortality 29%

Bitar FF. Acta Paediatr 2000;89:427
ICE in Lebanon

American University of Beirut Medical Center
300 bed tertiary care center in Beirut, Lebanon
TEE and cardiac surgery readily available

Joined ICE in 1999; 70 patients enrolled
In 2001, retrospective study of all cases of endocarditis since 1986

Streptococci major etiologic agents
Rheumatic heart disease most common predisposing condition
# Baseline Characteristics

<table>
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<th>No. of patients</th>
<th>n = 155</th>
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<tr>
<td>Age in years, mean (range)</td>
<td>52 (13-89)</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>105 (67.7)</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>21 (13.5)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (14.2)</td>
</tr>
<tr>
<td>CAD/CHF</td>
<td>16 (10.3)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>11 (7.1)</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>6 (3.9)</td>
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## Risk Factors for Endocarditis

<table>
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<tr>
<th>Risk Factor</th>
<th>n (%)</th>
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<tr>
<td>Invasive procedures</td>
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</tr>
<tr>
<td>Dental procedures</td>
<td>21 (13.5)</td>
</tr>
<tr>
<td>Other procedures</td>
<td>18 (11.6)</td>
</tr>
<tr>
<td>Devices</td>
<td></td>
</tr>
<tr>
<td>Pacemaker/ICD</td>
<td>8 (5.2)</td>
</tr>
<tr>
<td>Short-term central catheter</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>Chronic central catheter</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Predisposing cardiac conditions</td>
<td></td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>13 (8.4)</td>
</tr>
<tr>
<td>Rheumatic heart disease</td>
<td>26 (16.8)</td>
</tr>
<tr>
<td>Prosthetic valve</td>
<td>36 (23.2)</td>
</tr>
<tr>
<td>History of IE</td>
<td>17 (11.0)</td>
</tr>
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</table>

**Nosocomial acquisition:**

\[
\frac{17}{155} = 11.0\% 
\]
Microbiology

Streptococci 43%
Staphylococci 34%
Enterococci 12%
GNR 7%
Candida 2%
HACEK 2%

Culture-negative endocarditis: 30/152 = 20%

N = 52
- viridans strep (n = 40)
- β-hemolytic strep (n = 4)
- S. bovis group (n = 8)

N = 42
- MSSA (n = 21)
- MRSA (n = 7)
- CoNS (n = 14)

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# Echocardiography

<table>
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<th>Valve</th>
<th>n (%)</th>
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<tr>
<td>Mitral</td>
<td>80 (52.6)</td>
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<tr>
<td>Aortic</td>
<td>50 (32.9)</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>17 (11.4)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Concomitant left and right-sided IE</td>
<td>8 (5.2)</td>
</tr>
</tbody>
</table>

Evidence of IE on TTE/TEE: 123/152 = 81%

Medical Therapy

Beta-lactam monotherapy
N = 34 (21.9%)

Beta-lactam + aminoglycoside
N = 64 (41.3%)

Glycopeptide monotherapy
N = 5 (3.2%)

Glycopeptide + aminoglycoside
N = 5 (3.2%)

Other combinations
N = 41 (26.4%)
Surgical Treatment

- Surgery performed in 50 patients (32%)
- Mean time to surgery: 14 d (range 1-60 d)
- 56 valve replacements: 82% mechanical, 18% bioprosthetic
- Indications:
  - Valvular regurgitation: 78%
  - Vegetations: 44%
  - Heart failure: 36%
## Outcomes

<table>
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<th>Complication</th>
<th>N (%)</th>
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<tr>
<td>Death</td>
<td>24 (15.5)</td>
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<tr>
<td>Other complications</td>
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<tr>
<td>Congestive heart failure</td>
<td>32 (20.6)</td>
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<tr>
<td>Systemic embolization</td>
<td>28 (18.1)</td>
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<tr>
<td>Stroke (embolic and hemorrhagic)</td>
<td>17 (11.0)</td>
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<tr>
<td>Intracardiac abscess</td>
<td>12 (7.7)</td>
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Conclusions

- Epidemiology of IE in the ME is largely based on single-center studies
- More global studies are warranted
- Variation in microbiology
- Significant rates of culture-negative endocarditis
- Outcome is still poor in most cases