Hepatitis C virus infection in the Middle East and North Africa: A public health perspective

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The discovery in 1989

- A new virus, now called *hepatitis C virus*, was discovered

(Kuo et al, *Science* 1989) &
Global HCV prevalence

- Prevalence is about 0.1-3% across countries
Hepatitis C virus transmission

HCV is mainly transmitted through parenteral exposures such as sharing of injections or blood transfusion
The epidemiology of a new infection

- Populations affected are those exposed to blood products
- High-risk groups include: dialysis patients, injecting drug users, and multi-transfused patients such as hemophiliacs and thalassemics
A surprising discovery

• Routine blood-donor screening in Riyadh, Saudi Arabia
• Among Egyptian blood donors, HCV prevalence was 19.2%
• Every other nationality is <2.5%

(Saeed et al, Lancet, 1991)
The first study in Egypt

- Among university student blood donors, HCV prevalence was 10.9% (Kamel et al, *Lancet*, 1992)
HCV prevalence in Egypt

- Subsequent studies found prevalence levels as high as 50% among general population groups specially in the Nile Delta

(Frank et al, Lancet, 2000)
Abdel Halim Hafez
Why Egypt?
A painful discovery

- *Frank et al* were able to link the HCV epidemic to the parenteral antischistosomal therapy (PAT) mass-treatment campaigns mainly from 1960 to 1985

Sharing of non-sterilized injections
An observation by a WHO official

“Patients are … lined up in queues for … injection… The skillful doctor began injecting at 9.20 am and completed 504 injections of men, women and children by 10.10 am.”

BG Maegraith, *WHO Report*, 1964
A first in the history book

“The world's largest iatrogenic transmission of blood-borne pathogens known to date”

Hepatitis C virus disease progression

Course of illness with Hepatitis C

- Acute infection
- Chronic inflammation of the liver
- Fibrosis
- Cirrhosis of the liver
- Cancer of the liver

80% chance of cure
Hepatitis C virus disease progression

- Disease progression of chronic HCV infection:
  - 10% per year progression rate from one fibrosis stage to the next
  - 10-20% of chronically infected HCV individuals will develop cirrhosis within 20 years of infection
  - 1-3% of chronically infected HCV individuals will develop liver cancer within 30 years of infection
Number of deaths/year from selected conditions, Global Burden of Disease Study 2010 and 2013


Thanks to Dr Gottfried Hirnschall
Coming back to Egypt
Questions to be answered

• Key questions:
  – To what extent is HCV transmission still ongoing?
  – What are the modes of exposures to HCV in Egypt today?
An estimate of incidence among the living Egyptian cohort

- The incidence levels are suggestive of endemic and intense ongoing HCV transmission

(Miller and Abu-Raddad, PNAS, 2010)
Systematic review and data synthesis of HCV data

- Ongoing transmission in medical settings

(Mohamoud et al, *BMC Infectious Diseases*, 2013)
Clustering of HCV infection in Egypt

Clusters with high (A) and low (B) HCV prevalence

(Cuadros et al, *Hepatology*, 2014)
Multiple modes of exposure

- Multiple modes of HCV exposure appear to be present and mainly linked to medical care
HCV infection in other countries in the Middle East and North Africa (MENA)?
MENA HCV Epidemiology Synthesis Project

Aims of HCV Synthesis Project:

1. To describe analytically HCV epidemiology across MENA

2. To estimate the national population-level HCV prevalence in each MENA country

3. To estimate the number of HCV infected individuals in each MENA country
MENA sub-regions
HCV incidence
HCV incidence among clinical high risk populations- Fertile Crescent

Table 1. Studies reporting hepatitis C virus (HCV) incidence in countries of the Fertile Crescent region.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Year of data collection</th>
<th>Study site</th>
<th>Population</th>
<th>Study design</th>
<th>Sample size at recruitment</th>
<th>Lost to follow-up</th>
<th>HCV sero-conversion risk (relative to total sample size)</th>
<th>Duration of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bateha, 07 [37]</td>
<td>2003</td>
<td>Dialysis units/ National</td>
<td>Hemodialysis patients</td>
<td>Ret. cohort</td>
<td>1300</td>
<td>NA</td>
<td>9.2%</td>
<td>12 months</td>
</tr>
<tr>
<td>Iraq</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al-Rubaie, 11 [38]</td>
<td>2009</td>
<td>Hospital</td>
<td>Hemodialysis patients</td>
<td>Pros. cohort</td>
<td>57</td>
<td>0</td>
<td>40.3%</td>
<td>12 months</td>
</tr>
<tr>
<td>Al-Jadiry, 08 [40]</td>
<td>2007</td>
<td>Hospital</td>
<td>Pediatric patients with acute lymphoblastic leukemia Newborns to HCV infected women</td>
<td>Pros. cohort</td>
<td>123</td>
<td>0</td>
<td>3.2%</td>
<td>30 months (median)</td>
</tr>
<tr>
<td>Al-Kubaisy, 06 [42]</td>
<td>2006-07</td>
<td>Hospital</td>
<td>Pediatric cancer patients on chemotherapy Healthy children</td>
<td>Pros. cohort</td>
<td>85</td>
<td>22</td>
<td>3.2%</td>
<td>12 months</td>
</tr>
<tr>
<td>Al-Ali, 14 [39]</td>
<td>2007-09</td>
<td>Hospital</td>
<td>Pediatric patients with leukemia on chemotherapy</td>
<td>Pros. cohort</td>
<td>60</td>
<td>0</td>
<td>0%</td>
<td>6 months</td>
</tr>
<tr>
<td>Al-Ani, 11 [41]</td>
<td>2007-09</td>
<td>Hospital</td>
<td>Pediatric patients with leukemia who have had their baseline screening prior to chemotherapy</td>
<td>Pros. cohort</td>
<td>29</td>
<td>0</td>
<td>3.5%</td>
<td>6 months</td>
</tr>
<tr>
<td>Al-Ani, 11 [41]</td>
<td>2007-09</td>
<td>Hospital</td>
<td>Pediatric patients with leukemia</td>
<td>Pros. cohort</td>
<td>27</td>
<td>0</td>
<td>0%</td>
<td>6 months</td>
</tr>
</tbody>
</table>

*Abbreviations: Pros: prospective, Ret: retrospective.

(Chemaitelly et al, under review)
HCV prevalence
HCV prevalence among populations at high risk- Arab Maghreb

- **High** HCV prevalence indicating transmission in clinical settings and among PWID
- Including:
  - Hemodialysis patients
  - Hemophilia patients
  - Thalassemia patients
  - Multi-transfused patients
  - People who inject drugs
- Range of HCV prevalence:
  - Algeria: 30% (1 study)
  - Libya: 0-94.2% (9 studies)
  - Mauritania: No data
  - Morocco: 2.3-76% (9 studies)
  - Tunisia: 4.7-50.5% (17 studies)

HCV prevalence among the general population - Arabian Gulf

- **Low** HCV prevalence for the majority of measures.

  - Including:
    - Blood donors
    - Pregnant women
    - Children
    - Outpatient clinics’ attendees
    - Other general population

- Range of HCV prevalence:
  - Bahrain: 0.3% (2 studies)
  - Kingdom of Saudi Arabia: 0%-34% (269 studies)
  - Kuwait: 0.1%-14.0% (29 studies)
  - Oman: 0.4%-0.9% (2 studies)
  - Qatar: 0.3%-11.2% (4 studies)
  - UAE: 0%-3.6% (7 studies)

(Mohamoud et al, *ongoing work*)
HCV in Pakistan

National population-based survey
- HCV prevalence measured at 4.8%


Documented modes of HCV exposure in MENA
Exposures to HCV in medical settings

Medical settings exposures:
- Hemodialysis
- Blood transfusions
- Invasive clinical procedures
- Hospitalization
- Injections
- Dental work
- Women during child birth/miscarriage
Exposures to HCV in communities

- Community and informal health-provider related exposures:
  - Cupping (*hijama*)
  - Cautery
  - Tattooing
  - Shaving at barber shops
  - Circumcision (for females)
  - Injections administered by non-healthcare professionals
Mother to child transmission

- Mother to child transmission is a significant contributor to HCV incidence in Egypt
- Contribution could be also significant in Pakistan
- This mode of transmission seems limited in other countries

(Benova et al, *Hepatology*, 2015)
Exposure to HCV among people who inject drugs

- Evidence for sharing of needles/syringes as a risk factor for HCV exposure
- As expected, HCV prevalence is high among PWID across MENA countries

Estimates for HCV prevalence and number of HCV infections in MENA
National population-level estimates of HCV prevalence

Preliminary results

HCV prevalence (%)
Number of HCV antibody positive persons in MENA: Preliminary estimates for the 15-59 years age group

- Egypt: 7.56 million
- Pakistan: 4.92 million
- Horn of Africa: 0.53 million
- Arabian Gulf: 0.46 million

The number of HCV antibody positive individuals in MENA is ~ **14.2 million**

- Iran and Afghanistan: 0.28 million
- Fertile Crescent: 0.11 million
- Arab Maghreb: 0.34 million
### Number of HCV chronically infected persons in MENA: Preliminary estimates for the 15-59 years age group

<table>
<thead>
<tr>
<th>Region</th>
<th>Estimated Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egypt</td>
<td>5.07 million</td>
</tr>
<tr>
<td>Pakistan</td>
<td>3.30 million</td>
</tr>
<tr>
<td>Horn of Africa</td>
<td>0.36 million</td>
</tr>
<tr>
<td>Arabian Gulf</td>
<td>0.30 million</td>
</tr>
<tr>
<td>Iran and Afghanistan</td>
<td>0.19 million</td>
</tr>
<tr>
<td>Fertile Crescent</td>
<td>0.07 million</td>
</tr>
<tr>
<td>Arab Maghreb</td>
<td>0.23 million</td>
</tr>
</tbody>
</table>

The number of HCV chronically infected individuals with HCV in MENA is ~ **9.52 million**
A *brave new world*...
Breakthrough in HCV treatment: Direct-acting antivirals (DAAs)

- Release of a new drug Sovaldi (Sofosbuvir) by Gilead in 2013
- Oral well-tolerated treatment
- Treatment duration: 12 weeks
- Efficacy: >90%
- Extremely expensive drug
  - $1000 per pill
  - $84,000 per 12-week treatment course

Sovaldi sales reached $10.3 billion by the end of 2014, which makes it the best-selling drug in the world in its first year on the market.
Breakthrough in HCV treatment: Direct-acting antivirals (DAAs)

- Daklinza (daclatasvir), Viekira Pak (combination), and Harvoni (combination of ledipasvir and sofosbuvir)
- Rapidly developing pipeline
- Recognized as one of the most impressive success stories in modern medicine
- Access to treatment is the main obstacle; Saudi Arabia pays currently $101,460 per treatment course
We have highly efficacious drugs, but they are unaffordable for the vast majority of humanity.
Breakthrough in access to treatment

- 99% discount for Egypt; < $1000 per treatment course
- Pakistan obtained a similar discount recently
- Generics are being produced with as little as $750 per treatment course
- Production costs may go down to as little as $101
- Patents are not likely to be granted by national bodies in MENA
The path forward...
Policy and Strategies

- The first *Global Health Sector Strategy on Viral Hepatitis* is being drafted
- Development of *National Strategic Plans for Viral Hepatitis* and possibly a *Viral Hepatitis Programs* for each country
Countries with National Viral Hepatitis Plans (NVHP, Oct 2014)

EURO
1. Kyrgyzstan
2. Moldova
3. France
4. United Kingdom
5. Ireland
6. Uzbekistan

AMRO
1. Colombia
2. Brazil
3. Argentina
4. Canada
5. Peru
6. USA

EMRO
1. Egypt
2. Iran
3. Lebanon
4. Bahrain

SEARO
1. DPRK
2. Indonesia

WPRO
1. Australia
2. Japan
3. Mongolia
4. New Zealand

Thanks to Dr Gottfried Hirnschall
Programmatic interventions: HCV Screening, testing and treatment

• HCV screening, testing, and treatment program
• Egypt National HCV treatment program:
  – One of the largest in the world
  – Over 400,000 treated
  – 835,291 registered in the new treatment program in just few months
• Birth cohort screening is a possibility
• Screening and treatment are cost-effective

Thanks to Dr Manal El-Sayed
Programmatic interventions: Blood safety

- Blood screening for hepatitis C virus by PCR
- Only about 25% of blood units are screened by PCR in Egypt; the rest by ELISA of unknown quality

World Blood Donor Day
Programmatic interventions: Injection safety

  - Shift to “smart” syringes by 2020
- Average number of injections per person/year in MENA is 4.3; the highest in the world
  - In Egypt it is 6.8
- Pilot program for “smart” syringes including Egypt
Programmatic interventions: Harm reduction for PWID

- Harm reduction expansion in the region
  - Needle/syringe exchange programs
  - Drug dependence treatment
- 626,000 people who inject drugs (PWID) in MENA
- Iran is a world leader in harm reduction
Programmatic interventions: Improved infection control

- Infection control is a major challenge that is not easy to overcome in settings of limited resources.
Conclusions

- Overall, HCV prevalence in the population at large in most MENA countries is about 1-3%, comparable to most countries globally, with the notable exceptions of Egypt and Pakistan.

- Healthcare-related exposures and injecting drug use are the major drivers of HCV incidence.

- New or improved strategies need to be implemented for
  - HCV screening, testing, and treatment
  - Blood safety
  - Injection safety
  - Harm reduction for PWID
  - Infection control

- HCV elimination is now feasible, and possibly as early as 2030.
Acknowledgement

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