The Egyptian National HCV Control Program - Outcomes and Challenges

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National Hepatology Institute
Ministry of Health
Global Prevalence of Hepatitis C

Hepatitis C prev.

- <1
- 1 - 2.49
- 2.5 - 4.99
- 5 - 10
- > 10
- No Data
Introduction

- Egypt has one of the world’s highest prevalence of Hepatitis C
- Unfortunately, till 2007 we did not have a national control program for control of viral hepatitis
In Egypt, a high homology of HCV subtypes, 96% of which is genotype 4a, strongly suggests a local epidemic of HCV throughout the general population.

This genotype would have existed almost 100 years ago and the current high prevalence is the result of a rapid spread during four decades since 1940s.

Tanaka et al, 2004
The risk factor for HCV transmission that specifically sets Egypt apart from other countries is a personal history of *parenteral antischistosomal therapy (PAT)*.

This intensive transmission established a large *reservoir* of chronic HCV infection, responsible for the high prevalence of HCV infection and current high rates of transmission.
A review of the Egyptian parenteral antischistosomal therapy (PAT) mass-treatment campaigns, discontinued only in the 1980s, show a very high potential for transmission of blood-borne pathogens.

(FRANK ET AL., 2000; LANCET)
## NEW INFECTIONS CONTINUE TO OCCUR:

- unscreened blood transfusions/products
- unsafe injections
- exposed health care workers
- hemodialysis
- failure to sterilize medical equipment
- dental and “traditional” medicine
- injection drug users
  - rare: high risk sexual practices, horizontal and perinatal transmission
The national committee for control of viral hepatitis was established by the Ministry of Health (MOH) in 2007

**Objectives:**
- National Survey & Burden of Disease
- Treatment Program
- Prevention
  - Awareness and media Campaign
  - Infection control
- Clinical Research
- Management of advanced liver disease
The main goals of the National Control Strategy

- Detect the prevalence and incidence of HBV and HCV
- Reduce the prevalence of chronic HBV and HCV infection by 20% of 2008 levels by 2012
- Expand access to treatment to within 100 km for all Egyptians and treat 50% of persons needing treatment by 2014.
- Continue to produce high-quality scientific research
- Ensure program sustainability
Objectives

- National Survey & Burden of Disease
- Treatment Program
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NATIONAL HCV SURVEY
EGYPT 2009
Survey Partners

- Under auspices of Ministry of Health.
- Implemented by El-Zanaty in association with Demographic and Health survey (DHS) Egypt and MACRO international
- Funding from USAID and UNICEF.
- Hepatitis C testing undertaken at the central Laboratory of MOH with external quality assurance at the Theodor Bilharz Research Institute.
## Survey Parameters

- Hepatitis C knowledge
- Self reported prevalence of HCV
- Hepatitis C testing
  - Protocol
  - Coverage
  - Return of results
- Prevalence of HCV
- Disease Burden
Hepatitis C testing

- Household survey in 28 governorates.
- Total of 12,780 women and men aged 15 – 59 consented to blood sampling.
- Venous blood samples, frozen in liquid nitrogen containers, and transported twice weekly to Central Laboratory in Cairo for testing.
# Egypt HCV Survey 2009
## Knowledge of Hepatitis C

<table>
<thead>
<tr>
<th></th>
<th>Women %</th>
<th>Men %</th>
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<tbody>
<tr>
<td>Know about HCV</td>
<td>79</td>
<td>85</td>
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<tr>
<td>Source of knowledge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Television</td>
<td>93</td>
<td>88</td>
</tr>
<tr>
<td>Friends / Relatives</td>
<td>23</td>
<td>29</td>
</tr>
<tr>
<td>Know about transmission</td>
<td>70</td>
<td>78</td>
</tr>
<tr>
<td>Ever tested for HCV</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Ever treated for HCV</td>
<td>0.4</td>
<td>1</td>
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</table>
Testing Protocol

- ELISA test used to determine presence of antibodies.
- Real time PCR used for testing for HCV RNA for all antibody positive samples to detect infections in active phase.
- External quality control conducted for 2% of ELISA negatives, 5% of PCR positives and all PCR negatives.
Hepatitis C Testing: Findings

- HCV Antibodies detected in 14% of all individuals tested and evidence of active infection (positive PCR) detected in 9.8%.
- Infection rates rise sharply with age; persons 50 years and older 7-8 times more likely to be infected than individuals under age 30.
- Prevalence in males higher than females.
Hepatitis C Testing: Findings  cont.

- Rural rate 80% higher than urban rate.
- Lower Egypt the highest level and Frontier Governorates the lowest.
- Individuals reporting schistosomiasis treatment had very high infection rate.
Prevalence of Hepatitis C, Egypt 2009

<table>
<thead>
<tr>
<th></th>
<th>HCV antibody</th>
<th>HCV RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Women</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Men</td>
<td>17</td>
<td>11</td>
</tr>
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</table>
Prevalence of Hepatitis C by Age in Egypt 2009
Prevalence of Hepatitis C by self-reported Treatment (Injection) for Schistosomiasis, Egypt 2009
Geographic HCV prevalence

Alexandria 5.9%

Lower Egypt 28.4%

Middle Egypt 26.5%

Upper Egypt 19.4%

Cairo 8.9%
HCV prevalence and Residence

**Women**
- HCV RNA Positive: 8%
- HCV AB Positive: 15.2%

**MEN**
- HCV RNA Positive: 9%
- HCV AB Positive: 21.1%

Urban vs Rural Comparison:
HCV prevalence and Education

WOMEN

MEN

<table>
<thead>
<tr>
<th>Education Level</th>
<th>HCV AB % Positive</th>
<th>HCV RNA % Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Education</td>
<td>21.7</td>
<td>14.5</td>
</tr>
<tr>
<td>Some Primary</td>
<td>16.1</td>
<td>10.1</td>
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<tr>
<td>Primary Complete/Some Secondary</td>
<td>7.1</td>
<td>4.3</td>
</tr>
<tr>
<td>Secondary Complete / Higher Secondary</td>
<td>6.7</td>
<td>4.1</td>
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<table>
<thead>
<tr>
<th>Education Level</th>
<th>HCV AB % Positive</th>
<th>HCV RNA % Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Education</td>
<td>30</td>
<td>21.6</td>
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<tr>
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<td>15.2</td>
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<tr>
<td>Primary Complete/Some Secondary</td>
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<td>10.6</td>
</tr>
<tr>
<td>Secondary Complete / Higher Secondary</td>
<td>13.9</td>
<td>9.7</td>
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</table>
HCV prevalence and medical procedures

WOMEN

<table>
<thead>
<tr>
<th>Procedure</th>
<th>HCV AB %</th>
<th>HCV RNA %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SURGERY</td>
<td>13.6</td>
<td>9.2</td>
</tr>
<tr>
<td>BLOOD Tx</td>
<td>14.1</td>
<td>8.6</td>
</tr>
<tr>
<td>DENTAL</td>
<td>25.3</td>
<td>16.7</td>
</tr>
<tr>
<td>ANTI SCHISTO INJECTION</td>
<td>12.2</td>
<td>7.9</td>
</tr>
<tr>
<td>INJECTION FOR OTHERS</td>
<td>15.3</td>
<td>7.3</td>
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MEN

<table>
<thead>
<tr>
<th>Procedure</th>
<th>HCV AB %</th>
<th>HCV RNA %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SURGERY</td>
<td>22.1</td>
<td>15.5</td>
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<tr>
<td>BLOOD Tx</td>
<td>26.7</td>
<td>18.2</td>
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<tr>
<td>DENTAL</td>
<td>31.5</td>
<td>21.1</td>
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<tr>
<td>ANTI SCHISTO INJECTION</td>
<td>17.9</td>
<td>12.4</td>
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<tr>
<td>INJECTION FOR OTHERS</td>
<td>31.8</td>
<td>26.7</td>
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<tr>
<td>REUSED SYRINGES</td>
<td></td>
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HCV prevalence and wealth
Multivariate regression was used to estimate independent effects of risk factors on seropositivity of HCV.

Among those over 20 years of age, the following risk factors were significantly associated with seropositivity:

- Age
- Male gender
- Anti-schistosomiasis treatment
- Blood transfusion
- Invasive medical procedure (surgery, catheterization, endoscopy, and/or dialysis)
- Receipt of injections from "informal" health care provider
- Cesarean section or abortion
Those infected with HCV 100%

6-7 weeks incubation

No or only mild flu-like symptoms 70-80%

Acute Hepatitis 20-30%

Progression to chronic infection 75-85% (Our Data 50-60%)

Active liver disease (elev. ALT) 48-56%

Clearance 15-25%

Normal ALT 24-32%

Cirrhosis 8-16%

⇒ > 50% develop chronic active liver disease
⇒ 10-15% develop cirrhosis and hepatocellular carcinoma

HCC 1-4%

In HBV: 80% of those infected do not progress to chronic hepatitis
Objectives

- National Survey & Burden of Disease
- **Treatment Program**
  - Prevention
    - Awareness and media Campaign
    - Infection control
- Clinical Research
- Management of advanced liver disease
Patient management

- Scaled-up case detection efforts via voluntary counseling and testing.

- Improved access to treatment, including the opening of Viral Hepatitis Treatment Centers (VHTC) : 22 centers Nation-wide

- Reductions in the price of drugs, and expanded subsidization of antiviral therapy.

- Attaining optimal clinical management of all patients, (including pediatric patients and persons suffering from advanced liver disease)
HCV treatment centers
National Guidelines for the Treatment of Chronic HCV (2007)

- Age is from 18 to 60 years.
- The patients must be HCV RNA (PCR) positive.
- BMI ≤ 35
- Liver biopsy in every patient except:
  - Medical and paramedical Personnel
  - Genotype 2 & 3
  - Extrahepatic manifestations of HCV
Liver biopsy (Metavir score)

- F0: Treated if ALT is elevated or ≥ A2.
- F1: treated if ALT is elevated or ≥ A2.
- F2: treated.
- F3: treated.
- F4: only those with Child-Pugh class A and NO VARICES are treated.
Discontinuation of Treatment

Patients will receive antiviral therapy for 48 weeks unless:

- At 12 weeks: treatment is discontinued for patients who do not show a 2 log decrease in HCV RNA.
- At 24 weeks: treatment is discontinued for any patient with detectable HCV RNA by real time PCR.
- At 36 weeks: treatment is discontinued for any patient with a breakthrough.
National Guidelines for the Treatment of Chronic HCV (2007)

Dose of Antiviral Therapy:

Dose of Interferon :
- Peg-IFN alpha-2a
  180ug sc once weekly
- Peg-IFN alpha-2b
  1.5ug/kg sc once weekly

Dose of Ribavirin :
- <75kg : 1000mg/day
- ≥75kg : 1200mg/day
Modification of the National guidelines for the Treatment of Chronic HCV (2010)

- Patients with pEVR achieved a low SVR (<30%) with 48 weeks of therapy, so the decision was not to continue therapy to these patients.

- Patients with a BMI over 30 showed a low SVR (30%) and were treated after they lost weight.

- Patients with a METAVIR F4 showed a low SVR (20%) and were not treated on the modified national guidelines.
National Regulations for the Treatment of Chronic HCV

BEFORE Modification
- F0: Treated if ALT is elevated or ≥ A2.
- F1: treated if ALT is elevated or ≥ A2.
- F2: treated.
- F3: treated.
- F4: only those with Child-Pugh class A and NO VARICES are treated.
- BMI ≤ 35.
- Treatment continued for patients with pEVR.

AFTER Modification (2010)
- F0: Not treated.
- F1: treated if ALT is elevated or ≥ A2.
- F2: treated.
- F3: treated.
- F4: not treated.
- BMI ≤ 30.
- Treatment discontinued for patients with pEVR.
National Network for Treatment Centers (NNTC)

- A Network for all patients’ data from the Viral Hepatitis Treatment Centers nation-wide, was established with the main server located in National Hepatology Institute in Cairo.

- When fully functioning, the NNCTC will have full data for pre-enrollment and treatment of 150,000 HCV patients.
NNTC Requirements

1. Hardware
2. Software
3. Connection
4. Training
5. Implementation
What has been achieved

Training

Physician training
- lectures

Data Entry personnel
- workshops
  - Hands-on training
NNTC
Data Journey

Physician

Forms revised (date, physician name, Pt ID)

Data room

Nurse collects all forms

Forms to data entry employee

HQ

Data entry on computer

Given to nurse

Signed

Data written
National HCV Treatment Program

METHOD OF PAYMENT

- Government expenses, 38%
- Institute of health insurance, 51%
- Private health insurance, 3%
- Cash, 8%
National HCV Treatment Program

Method of Payment: centers

<table>
<thead>
<tr>
<th>Facility</th>
<th>Cash</th>
<th>Contract</th>
<th>Health Insurance</th>
<th>Governmental</th>
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<td>TMRI</td>
<td>186</td>
<td>79</td>
<td>2</td>
<td>485</td>
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<tr>
<td>Fatemic hospital</td>
<td>68</td>
<td>73</td>
<td>22</td>
<td>412</td>
</tr>
<tr>
<td>Kabary Alex</td>
<td>42</td>
<td>52</td>
<td>10</td>
<td>464</td>
</tr>
<tr>
<td>Tanta</td>
<td>18</td>
<td>44</td>
<td></td>
<td>552</td>
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National HCV Treatment Program

Type of IFN

<table>
<thead>
<tr>
<th>Hospital</th>
<th>IFN A</th>
<th>IFN B</th>
<th>Pending</th>
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<tbody>
<tr>
<td>TMRI</td>
<td>310</td>
<td>341</td>
<td>138</td>
</tr>
<tr>
<td>Fatemic</td>
<td>272</td>
<td>342</td>
<td>0</td>
</tr>
<tr>
<td>Kabary Alex</td>
<td>291</td>
<td>226</td>
<td>73</td>
</tr>
<tr>
<td>Tanta</td>
<td>95</td>
<td>356</td>
<td>5</td>
</tr>
</tbody>
</table>
National HCV Treatment Program: Outcome

EARLY VIROLOGICAL RESPONSE (12 WKS)

- NEG: 73%
- LOGs2: 6%
- POS: 21%

PERCENT
National HCV Treatment Program

Early virological Response (12 weeks): centers

TMRI: 83% (2/31 pending, 156 PCR -ve)
Fatemic hospital: 90% (3/15 pending, 134 PCR -ve)
Kabary Alex: 99% (16/16 pending, 277 PCR -ve)
Tanta: 96% (9/9 pending, 181 PCR -ve)

N.B: EVR is Per protocol, missing patients excluded
National HCV Treatment Program: Outcome

VIROLOGICAL RESPONSE (24 WKS)

PERCENT

%0.00 %20.00 %40.00 %60.00 %80.00

PCR RESULT

NEG  POS

%69.90 %30.10
National HCV Treatment Program: Outcome

END OF TREATMENT RESPONSE (48 WKS)

PERCENT

NEG  POS
%69.90  %30.10

PCR RESULT
National HCV Treatment Program: Outcome

SUSTAINED VIRAL RESPONSE

PERCENT

NEG

POS

PCR RESULT

%51.40

%48.60
Governmental appreciation of the magnitude of HCV problem in Egypt
National guidelines for treatment of chronic HCV
MOH and universities cooperation
Different specialties cooperation
Treatment for more than 145,000 patients
>90% governmental funding
Data to answer a lot of questions
Questions to be answered

- Stoppage rules
- Duration of therapy
- Cost effective analysis
- Non invasive detection of hepatic fibrosis
- Effect on disease progression
- Treatment of non responders
- HCV recurrence Post LTx
National HCV treatment program: Negative outcomes

- Quality control
- Individualization and personalization
- Funding
- Shortage of drugs
- Stoppage rule
- Non responders
- No guidelines for special groups
Acknowledgement

- **National Committee for Control of Viral Hepatitis**
  - (Mostafa Kamal, Manal Hamdy, Nasr El Sayed, Arnaud Fontanet, Gamal Esmat and Wahid Doss)

- **Advisory Board for Management of HCV**
  - (Sherif AFattah, Shoukry Hunter, Ali Monis, AR El Zayadi, A D El Sehly, Seham A Rehim and A M Nasr)
Hepatitis C remains a major health problem in Egypt with 9% of the population chronically infected.

The national HCV control program has been effective in providing treatment nationwide for almost 145,000 patients.

Methods for prevention of new infections need to be intensified.