Hepatitis C and B in Thalassemia patients
From Epidemiology, diagnosis, treatment to prevention strategies

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Learning objectives:

After this presentation, you will understand:

• The Importance of HCV infection in Thalassemia
• The Burden of HCV infection in Thalassemia in Iran and the region
• Prevention strategies
• Treatment of HCV infection in Thalassemia
• And where we are standing now and the Future!
Thalassemia Patients are special patients

Special patient populations require special care
Patients with thalassemia or other hemoglobinopathies were at greater risk of acquiring HCV infection as a consequence of repeated transfusions of blood, respectively, before the introduction of blood donor screening for hepatitis C.
Previously Thalassemia patients died as consequences of cardiovascular diseases and infections and because of low life expectancy liver diseases caused by iron overload or HCV/HBV infection did not get the chance to manifest itself.

However today, longer life expectancy are turning liver diseases to the third cause of morbidity and mortality in thalassemia patients.
Importance of HCV Infection in Thalassemia Patient

- High prevalence and burden of disease
- Synergic effects of iron overload and HCV infection on induction of liver fibrosis
- Role of iron on yielding IFN resistance and lowering of hepatitis C viral clearance

Risk Factors of HCV Progression to Cirrhosis

- Male gender
- Age above 40
- Alcohol consumption
- Increased activity and fibrosis
- **Increased hepatic iron**
- Duration
- Other hepatotropic viruses

HCV IN THALASSEMIA: THE IMPORTANCE OF IRON OVERLOAD ON FIBROSIS PROGRESSION

Angelucci et al. Blood 2002
In Iran from a total of 5229 thalassemia subjects, its Seroepidemiology ranged from 2 to 32%. Pooled HCV infection rate was 18%.

**Pooled HCV infection rate**
- 45% in Pakistan
- 63% in Saudi Arabia
- 69% in Egypt

**In Iran, blood donors screening for HCV infection started in 1996. The pooled OR of HCV infection rate for patients transfused before that date was OR=7.6 and this implies an increase in blood safety and more attention to health precautions in Iran.**

Hepatitis C in Thalassemia Patients

• After initiation of donors screening for HCV in 1995 and exclusion of high-risk groups from donation pool, the prevalence of HCV infection in thalassemia patients had decreased significantly in Iran.

Alavian SM, et al. The efficacy of blood donor screening in reducing the incidence of hepatitis C virus infection among thalassemic patients in Iran. Transfusion Today. 2002
Nosocomial Transmission of Hepatitis C at Iranian Thalassemia Centers

• Strains in seven clades were from nine patients infected between 1999 and 2005 and similar to strains from eight patients infected before 1996, indicating ongoing transmission at the centers.

• Further epidemiological investigation revealed that 28 patients infected with strains within the same clade had frequently been transfused at the same shift sitting on the same bed.

• An additional eight patients with related strains had frequently been transfused simultaneously in the same room.

• **Nosocomial transmission at these thalassemia centers both before and after the introduction of blood screening. Further training of staff and strict adherence to preventive measures are thus essential to reduce the incidence of new HCV and TREATMENT OF ALL PATIENTS WITH NEW DRUGS**
Hepatitis C Genotypes in Iran

HCV Genotypes in General Population

HCV Genotypes in Thalassemia

TABLE 2. Distribution of genotypes among Iranian population with thalassemia with HCV infection

<table>
<thead>
<tr>
<th>HCV genotype</th>
<th>Number of isolates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>146 (52)</td>
</tr>
<tr>
<td>1a and 1b</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>1a and 3a</td>
<td>4 (1.4)</td>
</tr>
<tr>
<td>1a and 3b</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>1b</td>
<td>14 (5)</td>
</tr>
<tr>
<td>2a</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>3a</td>
<td>97 (34.5)</td>
</tr>
<tr>
<td>3a and 1b</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>3a, 1a, and 1b</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>3b</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>3a, 4</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Nontypeable</td>
<td>7 (2.5)</td>
</tr>
</tbody>
</table>

Transient Elastography by Fibroscan®

Advantages

• Non-invasive and painless
• Quick
• Evaluation of larger area reduces sampling errors
• Best at identifying significant fibrosis

Limitations

• Poor discrimination in mild-to-moderate fibrosis
• Cannot be used in patients with ascites
• Inaccurate in obese patients
We are serious regarding control of hepatitis C in I.R.Iran
HCV in Thalassemia is on control in Iran now
How?

I hope for future to support more for new drugs and tomorrow HCV will be eliminated!
• In a meta-analysis determined that addition of ribavirin to conventional IFN increases SVR rates by twofold, from 30% to 61%, similar to non-thalassaemic patients.

• We also determined that Genotype 1-infected patients significantly benefit from the addition of ribavirin to IFN monotherapy.
Ribavirin Has Not Approved Yet!

- Ribavirin that is in front line of HCV infection therapy is not approved in thalassemia patients because of its dose dependent hemolytic side effects, elimination of this drug from therapeutic regimen have decreased significantly rate of SVR in thalassemia patients.

Safety of Ribavirin in Thalassemia Patients

- It appears that administration of Ribavirin does not increase major adverse events and treatment discontinuation due to intractable side effects.

- Ribavirin increases transfusion needs by 30-50 percent that would return to pre-treatment level 2-3 months after end of treatment.

• Treatment of HCV infected patients is important strategy for control of HCV infection in thalassemia group.

• Sustained virological response (SVR) was significantly higher in patients who received ribavirin (51 % vs. 38 % P = 0.02). In multivariate regression, OR of ribavirin for prediction of SVR was 2.2 (95 % CI 1.24-3.91)
Conclusion

• Age, HCV type, serum ferritin, viral load and serum ALT are determinants of ribavirin administration benefit in thalassemia patients.

  • Ribavirin is completely safe and effective in thalassemia patients.

New Drugs are coming soon!
Direct Acting Antiviral Agents for Treatment of Hepatitis C Virus Infection

5' NTR → Structural proteins → Non-Structural proteins → 3' NTR

HCV polyprotein cleavage → Formaion of membranous web, Replication, Virus assembly → RNA dependent RNA polymerase

**NS3/4A Protease inhibitors (-previr)**
- Telaprevir
- Boceprevir
- Simeprevir
- Asunpravir
- Danoprevir
- Paritaprevir

**NS5A inhibitors (-asvir)**
- Daclatasvir
- Ledipasvir
- Ombitasvir
- Velpatasvir
- Ach-2928
- Ach-3102

**NS5B Polymerase inhibitors (-buvir)**
- PPI-668
- PPI-461
- GSK2336805
- Samatasvir
- BMS-824393
- BMS-791325
- PPI-383
- GS-9669
- TMC647055I
- VX-222

**Regimen**
- Harvoni + RBV
- Zepatier
- Viekira Pak

AbbVie's Regimen
Treatment Regimens

- Sofosbuvir (SOF)/ Pegylated Interferon (PEG)/Ribavirin (RBV)
- Sofosbuvir (SOF)/ Ribavirin (RBV)
- Sofosbuvir (SOF)/ Simeprevir (SIM)
- Ledipasvir (LDV)/ Sofosbuvir ±RBV
- Daclatasvir (DAC)/ Sofosbuvir ±RBV
- Ombitasvir (OMV) / Paritaprevir (PTV)/ Ritonavir (R)/ Dasabuvir (DSV)
- Ombitasvir (OMV) / Paritaprevir (PTV)/ Ritonavir (R)/ Ribavirin (RBV)
- Grazoprevir/Elbasvir
HCV treatment strategies: What is the Middle East’s Situation?

- PEG-IFN + RBV
- PEG-IFN + RBV + DAA
- IFN-free DAA combination
Elimination of HCV infection in Iran will be in 2030 but in thalassemia is possible in 2020!

Solution

Work together
   More support for therapy
   More attention to blood safety
   More education the nurses in thalassemia centers
Increase the thalassemia patients awareness regarding the issue.
Thanks for your attention