Effectiveness of Strategies for Control of Viral Hepatitis in Patients with Inherited Disorders of Hemoglobin in Sistan-Baluchistan Province, Iran; an Epidemiologic Study

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Introduction

- Regular and prolonged blood transfusion in patients with inherited disorders of hemoglobin (IDH), particularly thalassemia, exposed them to blood transmitted infection, including viral hepatitis. Implementation of effective vaccination of hepatitis B in 1980s and screening of blood products in 1990s resulted in remarkable reduction in hepatitis B virus (HBV) and hepatitis C virus (HCV) infections.
In Iran, since 1996 routine screening for blood-borne diseases has been mainly conducted among blood donors and due to this program, prevalence of HCV in thalassemia patients decreased significantly. Previous studies in Iran reported the seroprevalence of HCV in beta-thalassemia patients at a wide range of 7%-34% and prevalence of HBV from 0.3% to 7%.
Sistan-Baluchistan province located at southeast of Iran, bordering with Afghanistan and Pakistan. This province with more than 3000 cases of thalassemia has one of the highest prevalence of thalassemia in Iran. Moreover, this province has high prevalence of HBV infection with more than 3% prevalence of patients with HBsAg. Due to lack of sufficient reported data from Sistan-Baluchistan province, we conducted this multicentric study to provide a comprehensive data bank on epidemiology HBV and HCV infection in patients with IDH in Sistan-Baluchistan, furthermore we tried to analyzed data which allow the development of an effective policy to reduce the incidence of HBV and HCV infection in our patients with IDH.
Prevalence of hepatitis B virus among general population in Iran

- **East Azarbajyan**: 4207 (1.2%) Bayat 2000
- **Kurdistan**: 1613 (0.87%) Alavian
- **Hamedan**: 4930 (2.49%) Amini
- **Lorestan**: 454 (5.9%) Ali Papi 2013
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- **Hormozgan**: 1455 (2.7%) Merat 2007
- **Isfahan**: 816 (1.3%) Nokhodiyan 2005
- **Tehran**: 2327 (2.3%) Merat 2007
- **Golestan**: 1896 (5.1%) Merat 2007
- **Khorasan Razavi**: 3198 (1.0%) Shakeri 2010
- **Balochistan Province of Pakistan**: 1166 (9.8%) Nadeem S 2004-2008
- **Sistan Baluchestan**: 3989 (3.36%) Salehi 2008-2009

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**Legend**
- **Province Names**: Tehran, Isfahan, Hamedan, Lorestan, Hormozgan, Golestan, Khorasan Razavi, Balochistan Province of Pakistan, Sistan Baluchestan
- **Prevalence Values**: Represented in parentheses for each province
- **Years**: Indicate the year of study or publication
Prevalence of hepatitis C virus among general population in Iran

Amol, Mazandaran
6145 (0.2%)
Mansour-Ghahaei
2003

Tehran
2326 (0.3%)
Merat
2007

Golestan
1895 (1.0%)
Merat
2007

Kermanshah
1721 (0.87%)
Amini
2006

Lorestan
827 (0.2%)
Mohebbi
2007-2008

Sistan Baluchestan
2587 (0.5%)
Ansari-moghaddam
2008-2009

Ahvaz
712 (0.63%)
Nikbakht
2007-2008

Hormozgan
Merat
1463 (1.6%)
2007

Khorasan Razavi-Mashhad
3870 (0.2%)
Shakeri
2010-2011

Pakistan
4.7%
Analysis of 25 studies
2000-2008
Methods

In this retrospective study, a total of 2391 patients who referred thalassemia clinics in Sistan-Baluchistan province till April, 2016 were initially included. The inclusion criteria were:

1. Patients who had thalassemia or other inherited disorders of hemoglobin,

2. Patients who had permanent residence (more than 5 years) in Sistan-Baluchistan province,

3. Patient who had transfusion-dependent IDH with the need of more than once a year transfusion of packed cell
Detection of HBsAg and HCV Ab was performed in Iranian Blood Transfusion Organization, Zahedan, Iran. For detection of HBsAg patients’ sera were tested using Enzygnost HBsAg 6.0 (Siemens). Patients’ sera were tested using EIAGen HCV Ab (v.4) Kit(Adaltis) for evaluation of HCVAb. In a proportion of patients with positive result for HCV Ab, the HCV RNA detection and HCV genotyping was performed using valid methods in a private diagnostic laboratory. Moreover, the data of hepatitis B surface antibody (HBsAb) was extracted from patients’ records.
**Table 1. The characteristics of patients with inherited disorders of hemoglobin in Sistan-Baluchistan Province**

<table>
<thead>
<tr>
<th>Sex, n (%)</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2387</td>
</tr>
<tr>
<td>Female</td>
<td>1116</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years), mean±SD</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2376 ± 7.7</td>
<td>12.7 ± 7.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>City of residence, n (%)</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chabahar</td>
<td>452 (18.9)</td>
</tr>
<tr>
<td>Iranshahr</td>
<td>405 (17.0)</td>
</tr>
<tr>
<td>Khash</td>
<td>148 (6.2)</td>
</tr>
<tr>
<td>Nikshahr</td>
<td>136 (5.7)</td>
</tr>
<tr>
<td>Saravan</td>
<td>391 (16.4)</td>
</tr>
<tr>
<td>Zabol</td>
<td>184 (7.7)</td>
</tr>
<tr>
<td>Zahedan</td>
<td>671 (28.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of inherited disorders of hemoglobin, n (%)</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta thalasemia major</td>
<td>2249 (99.2)</td>
</tr>
<tr>
<td>Beta thalasemia intermedia</td>
<td>5 (0.2)</td>
</tr>
<tr>
<td>Others</td>
<td>14 (0.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Splenectomy, n (%)</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2364</td>
</tr>
<tr>
<td>No</td>
<td>2146</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diabetes, n (%)</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1650</td>
</tr>
<tr>
<td>No</td>
<td>1614</td>
</tr>
</tbody>
</table>
Discussion

This study investigated the prevalence of viral hepatitis B and C seromarkers in a large cohort of 2387 patients with IDH in Sistan-Baluchistan province and found 5.87% HCV seroprevalence and 0.29% HBV seroprevalence.

In Iran, HCV infection in thalassemia patients is more frequently observed than in general population mainly as a result of blood transfusion before 1996 when the donated bloods were not screened for HCV Ab. In a meta-analysis, the frequency of HCV Ab was between 2% to 32%
Prevalence of hepatitis C virus among Thalassemia in Iran

No of participants (prevalence)

- Sistan Baluchestan: 2387 (5.8%) - Khosravi 2016
- Mashhad: 360 (8.33%) - Mansouri 2007
- Qazvin: 96 (24.2%) - Alavian 2002
- Arak: 97 (9.2%) - Mahdaviani 2004
- Ahvaz: 206 (28.2%) - Ghafourian 2005-2006
- Shiraz: 466 (15.7%) - Karimi 1999-2000
- Kohgiloyeh and Boyerahmad: 49 (6.1%) - Sarkari 2009-2010
- Isfahan: 545 (5.6%) - Kalantari 2008-2010
- Kerman: 181 (44.7%) - Hassanshahi 2006-2007
- Yazd: 85 (9.4%) - Javadzadeh 2003
- Tehran: 395 (27.5%) - Azerkyvan 2009
- Semnan: 81 (24.4%) - Mirmomen 2002
- Pakistan: 1253 (27.5%) - Rizwan Ahmed Kiani 2016
among thalassemia patients in different provinces of Iran with pooled seroprevalence of 18% (8). The first study on seroprevalence of HCV in thalassemia patients in Sistan-Baluchistan province was conducted by SaneiMoghadam et al. (11) in 2004 with observation of 13.5% rate for positivity of HCV Ab in thalassemia. Implementation of screening for HCV Ab in donations after 1996, had great impact on lowering the rate of transfusion-transmitted HCV infection among thalassemia patients. The findings of the present study confirm the latter fact with observation of a drop from 17.2% of HCV seroprevalence in thalassemia patients aged 21-30 (born before 1996) to 5.1% in thalassemia patients aged 11-20 (born after 1996). However, HCV seroprevalence was high even in thalassemia patients born after 1996 with 5.1% in patients aged 11-20 and 1.9% in patients aged <11 which can be as a result of nosocomial transmission (12).
**Figure 1.** Seroprevalence of HCV in patients with inherited disorders of hemoglobin in relation to age

The rate of HCV seropositivity was significantly different between all age groups except between the groups of 21-30 and >30.
Trend HCVAb positive in blood donor in Sistan and Balochestan province
In the current study, HCV RNA was detected in 53% of HCV-seropositive IDH patients with available data for assessment of HCV RNA. In comparison with 25% spontaneous clearance found in most of the previous studies (15, 16), observation of 47% of HCV-seropositive IDH patients with negative result for HCV RNA should not be reliable and can be caused by the fact that some of the patients were treated for HCV infection previously or as a result of false positive result in HCV Ab testing by ELISA.
In this study, 72.5% of patients were infected with HCV genotype 3 and the remaining with HCV genotype 1. In Iran, HCV genotype 1 is the most prevalent HCV isolate (17, 18). Moreover, HCV genotype 1 was the most isolated genotype from Iranian thalassemia patients with HCV infection(19). However, a previous study in Sistan-Baluchistan found HCV genotype 3 as the dominant genotype in children and adolescents with major thalassemia(20).
The detection rate of HBsAg is less than 2% in Iran however Golestan and Sistan-Baluchistan provinces have HBV prevalence more than 2% \(^{(10)}\). It has been estimated that 3.38% of general population of Sistan-Baluchistan to be HBsAg-positive\(^{(21)}\). In this study, the prevalence of HBsAg in patients with IDH in Sistan-Baluchistan province was less than 0.5% which is unexpectedly much lower than general population of Sistan-Baluchistan. The low prevalence of HBV infection in Iranian patients with IDH was reported previously as well\(^{(1, 6)}\). The low seroprevalence of HBV in thalassemia patients can be as a result of HBV vaccination of infants and thalassemic patients as a high-risk group for transmission of HBV and also, increased mortality of patients with IDH and HBV infection.
The prevalence hepatitis B in thalassemia major at various geographic parts of Iran

<table>
<thead>
<tr>
<th>Provinces</th>
<th>No of individuals</th>
<th>HBsAg (No/%)</th>
<th>References</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central (Ghazvin)</td>
<td>95</td>
<td>1 (1.1%)</td>
<td>Alavian</td>
<td>2002</td>
</tr>
<tr>
<td>South –east (Sistan &amp; Baluchestan)</td>
<td>2387</td>
<td>7 (0.29%)</td>
<td>khosravi</td>
<td>2016</td>
</tr>
<tr>
<td>Central (Yazd)</td>
<td>85</td>
<td>0 (0%)</td>
<td>Javadzadeh</td>
<td>2003</td>
</tr>
<tr>
<td>Central (Kerman)</td>
<td>100</td>
<td>6 (6%)</td>
<td>Zahedi</td>
<td>2002</td>
</tr>
<tr>
<td>Central (Markazi)</td>
<td>97</td>
<td>0 (0%)</td>
<td>Mahdaviani</td>
<td>2004</td>
</tr>
<tr>
<td>South (Shiraz)</td>
<td>755</td>
<td>4 (0.53%)</td>
<td>Karimi</td>
<td>2000</td>
</tr>
<tr>
<td>North –East (Khorasan)</td>
<td>360</td>
<td>8 (2.2%)</td>
<td>Mansourii</td>
<td>2007</td>
</tr>
<tr>
<td>West (Kermanshah)</td>
<td>232</td>
<td>0 (0%)</td>
<td>Sayad</td>
<td>2015</td>
</tr>
</tbody>
</table>
Trend hepatitis B in blood donor in Sistan and Baluchistan province 2005-2016