Liver Transplantation for Viral Liver Disease in Israel

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Ministry of Health
The West Galilee Medical Center
Liver Transplantation in Israel

• Since 1991

• Three liver transplantation centers:
  – The ‘Rabin’ Medical Center
  – The Tel-Aviv Medical Center
  – The ‘Hadassah’ Medical Center
Liver Transplantation in Israel

• 840 liver transplantations

• Allocation scheme:
  – 1991-2002: Local
  – 2002- current: Central:
    • 2002-2005 The New England score
    • 2005-Current: The MELD score
Etiology for Liver Transplantation

* 1991-1999

Chronic Viral Hepatitis: 49%:
- HCV: 25%
- HBV: 19%
- HBV/HCV: 2%
- HBV/HDV: 3%


2006-2011**

Chronic Viral Hepatitis: 50.7%:
- HCV: 33.6% (HCC: 17%)
- HBV: 15.9% (HCC: 9%)
- HCV/HIV: 0.4%
- HBV/HDV: 0.4%


HCV: Hepatitis C; HCC: Hepatocellular carcinoma; HBV: Hepatitis B; HDV: Hepatitis D; ALF: Acute liver failure; NASH: Non alcoholic liver disease; ALD: Alcoholic liver disease; re-Tx: re-transplantation
Liver Transplantation for Hepatitis C:

• Men: 61.3%
• Average age\(^1\):*
  • Until 2006: 50.8±10.4
  • 2006-2011: 56.8±7.75
    *(p=0.015)*
• Demographic (candidates on waiting list\(^2\))
  • Eastern Europe: 58%
  • Native Jews: 16%
  • Native Arabs: 10%
  • North Africa: 8%
  • North America/ Europe: 8%

\(^1\)The Israeli National Transplant Center
\(^2\)Carmiel et IA SL meeting; 2009;
# Liver Transplantation for Hepatitis C Survival (1998-2009)

<table>
<thead>
<tr>
<th></th>
<th>Patient Survival</th>
<th>Graft Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 year (%)</td>
<td>3 year (%)</td>
</tr>
<tr>
<td>Non-HCV patients</td>
<td>83%</td>
<td>80%</td>
</tr>
<tr>
<td>(n=78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV patients (n=65)</td>
<td>81%*</td>
<td>74%*</td>
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</tbody>
</table>

* p<0.05

Early (90 days) mortality: 12.3%

Late mortality:

- **HCV related graft failure: 37.5%**
  - Recurrent HCV cirrhosis: 25%
  - Fibrosing cholestatic hepatitis: 12.5%
- Non-HCV related liver failure: 12.5%
- Other: 50%
Recurrence of Hepatitis C

- Evidence of recurrence: 63-72%*/**
- Median interval to recurrence: 117 days (19-488 days)
- Early stage HCV @ diagnosis: 96%*

Response to treatment:
- Introne + Ribavirin: SVR 1:10 (10%)
- Peg-interferone + Ribavirin:
  - Intent to treat SVR 5:20 (25%)
  - Per protocol SVR 5:11 (45.5%)
- Treatment with anti HCV Direct Acting Agents?

60% of responders had increased fibrosis despite SVR

*Carmiel et I IA SL meeting; 2009
**Shaharabani E. et al Harefuah, Sep. 2000
Liver Transplantation and Hepatitis C: Related Policy

• No re-transplantation for HCV related liver failure
• Exemption - rare

HCV (+) DONOR
• Use of anti HCV(+) donors for anti HCV(+) recipients
Liver Transplantation for Viral Liver Disease in Israel

Liver Transplantation for Hepatitis B

• Prevalence among liver transplant recipients:
  • 1991-1999: 19% (HDV 3%)*
  • 2006-2011: 15.9% (HDV 0.4%)**

• Demographics:
  • Native Arabs: 44%
  • Native Jews 12%
  • Eastern Europe: 13%
  • North Africa: 25%
  • Africa 6%

*Shaharabani E. et al Harefuah, Sep. 2000
** Carmiel M. Harefuah, Dec. 2012
***The Israeli National Transplant Center
Re-infection with Hepatitis B:

- **Pre nucleotide/side analog (NUC) era:**
  - Incidence of 35%* graft re-infection:
    - Mortality due to liver failure: 30%
    - YMDDD mutation early after starting Lamivudine
- **Since 2000:**
  - Re infection: rare

- **De Novo** Hepatitis B: Reported 5 cases:
  - HBcAB+ donor: 2
  - Iatrogenic: 1
  - Sexually transmitted: 1
  - Unknown: 1

*Shaharbani E.et al. Harefuah, 2000, 139(6)*
*Ben-Ari Z. Liver Transpl 2001, 7(2)*
Candidates Evaluation for HBV Infection

HBcAB

- Negative: Check for HBsAB
  - Negative: Vaccinate: Sci-B-vAC
  - Positive
    - Positive: Check for HBsAG
      - Positive: Check HDV: Check HBV PCR
        - Positive PCR: Start NUC
        - Negative PCR: Check Q3M
          - Anti HDV: Check PCR
        - Negative PCR: Check Q3M
Preventing HBV Re-Infection

**NUC Protocol**
- Continue NUC previously given
- Naïve HBsAg (+), HBV DNA(-): start Lamivudine
- Repeat HBV DNA check

**HBIG Protocol**
- Un-hepatic phase
- 3-7 days post operative
- According to HBsAB levels repeat when:
  - High risk pts.
  - First year
  - After 1st year → <100-150 u/ml
  - Check repeatedly for HBsAg + DNA

<500 u/ml
Liver Transplantation and Hepatitis B: Related Policy

- Pre transplantation HBV DNA – mandatory for non-urgent cases

**Use of HBcAb + Donors**

<table>
<thead>
<tr>
<th>Donor</th>
<th>HBsAg+</th>
<th>Isolated HBcAb</th>
<th>HBcAB+; HBsAb+ HBsAg−</th>
<th>HBcAb−, HBsAb+</th>
<th>HBcAb− HBsAb−</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBcAb+; HBsAg− HBsAb +</td>
<td>Yes</td>
<td>yes</td>
<td>yes</td>
<td>Yes*</td>
<td>+/-**</td>
</tr>
<tr>
<td>Isolated HBcAB</td>
<td>Yes</td>
<td>Yes*</td>
<td>yes</td>
<td>Yes*</td>
<td>+/-**</td>
</tr>
<tr>
<td>HBsAg +</td>
<td>Consider Bx</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>

• F/U HBsAb ** Nuc Rx. vaccinate., f/u HBcAb
Urgent Liver Transplantation due to Viral Hepatitis

Etiology for Urgent Liver Transplantation (Tel-Aviv Medical Center 2003-2009)

- Other: 33.3%
- Wilsonian crises: 14.3%
- HAV: 0%
- HEV: 4.8%
- HBV: 14.3%
- Non A-G hepatitis: 23.8%
- ACAP: 9.5%

*Carmiel. et al. AASLD, 2007 (abstract)*
Urgent Liver Transplantation due to Viral Hepatitis: Pediatric

- Hepatitis A: Leading cause for pediatric urgent liver Tx.

- All HAV cases before 1999

- No HAV induce liver failure was reported (March 2013)

Etiology for Urgent Pediatric Liver Transplantation 1996-2007

- HAV: 38; 38%
- Wilson's dis.: 31; 31%
- AIH: 8; 8%
- Unknown: 23; 23%

HAV: Hepatitis A; AIH: Autoimmune hepatitis

• Shouval et al. J Pediatr Gastroenterol Nutr. 48(4) 2009
Liver Transplantation for Viral Hepatitis in Israel: Future

Hepatitis C:
• Leading liver disease
• Older recipients

Post transplantation
• Universal recurrence
• New direct acting agents
• HCIG??

Candidates for Liver Transplantation March 2013

- HCV: 26%
- HBV: 15%
- HCV/HBV: 0.5%
- Other: 56.5%
Liver Transplantation for Viral Hepatitis in Israel: Future

Hepatitis B:

• Excellent outcome after transplantation

• Entecavir/Tenofovir:
  • Better viral control:
    – Less need for transplantation?
    – Lower incidence of HCC?
    – NUC mono-therapy to prevent re-infection?
Liver Transplantation for Viral Hepatitis in Israel: Future

Acute Liver Failure:

- Eradication of HAV
- Screening and preventive therapy for HBsAg + immune-compromised patients
Liver Transplantation is a Team Work

Tamar Ashkenazi and Rona Ben-Simon
The Israeli Transplant Center
Ministry of Health

Oren Shibboleths and Helena Katchman
Liver Unit
Tel-Aviv Medical Center

Rifaat Safadi
Liver Unit
Hadassah Medical Center

Marius Braun
Liver Unit
Rabin Medical Center

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The Organ Transplantation Center
Rabin Medical Center

Riki Shapira
Pediatric Liver Transplantation Unit
Schneider Children Hospital
Rabin Medical Center

Liver Transplantation for Viral Liver Disease in Israel