MEDICAL AND ECONOMIC BURDEN
OF CHRONIC HEPATITIS B PATIENTS
AT QUEEN SAVANG VADHANA MEMORIAL HOSPITAL

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A THESIS SUBMITTED FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
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INTRODUCTION

• 2-7% HBsAg prevalence, 1.3 to 4.5 million Thais are hepatitis B infections.

• One third or 0.4-1.5 million Thais will develop cirrhosis, hepatocellular carcinoma (HCC) (1).

CHB imposes a substantial economic burden on patients, families, and the society.

• In China, direct medical costs of CHB was USD 1,636 patient/year with exceeded 31 percent of the household income (2).

The medical and economic burden of Thai CHB patients has not been described.

1. Ott, JJ et al. 2012, Vaccine, 30, 2212-2219.;
OBJECTIVE & INCLUSION CRITERIA

OBJECTIVES

• To assess medical and economic burden of chronic hepatitis B (CHB) patients at twelve month of follow up

Inclusion criteria

Male or female with 18 years old and over.
Criteria for diagnosis and/ or treatment base on Thailand Consensus Recommendations for Management of Chronic Hepatitis B and C 2009.
Participant is willing to participate voluntarily.
Participant is willing and able to provide written informed consent to participate in the study.
MATERIAL AND METHODS

Study Design
A cohort study

Location of the study
At Queen Savang Vadhana Memorial Hospital, Chonburi province

Duration of the study
November 2011 to April 2013

Study population
CHB patients at all disease stages who visited OPD

Three forms & Three questionnaires:

Forms
- Source document
- Case record form (CRF)
- Transport and other expenditure form (TEF)

Questionnaires:
- EuroQol-5D (EQ-5D) (self-administering)
- Chronic Liver Disease Questionnaire (CLDQ) (self-administering)
- Work Productivity and Activity Impairment (WPAI) (interview)

All have been translated into Thai and permitted to use in this study that were applied three times; at D0, M6, and M12.
EQ-5D

Generic health related quality of life quest.
• Outcomes can be compare with others
• Takes 10 minutes
• Has 5 items 5 Dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression
• Each item has 3 levels of health impairment:
  1 = no health impairment,
  2 = some health impairments,
  3 = severe health impairments

EQ-5D VAS; 0-100 score health impairments
Liver disease specific questionnaire

- Takes 15 minute
- Has 29 items 6 domains:
  - Abdominal symptom (AB),
  - Fatigue (FA),
  - Systemic symptom (SY),
  - Activity (AC),
  - Emotional function (EM),
  - Worry (WO)
- Each item has 7 levels of severity:
  1 = All of the time or the most impairment to...
  7 = None of the time or the least impairment

The lesser score means the more severity,
The higher score means the less severity.
WPAI

Work productivity loss related health quest.

- Takes 5 minute
- Has 6 items
- Asks patients:
  
  **Impairment while working**, **Activity impairment**

  - Rates degree of impairment

  From the least 0 score to the most 10 scores

  % impairment

Least.................Most
### Validity and Reliability of the Questionnaires

<table>
<thead>
<tr>
<th>Questionnaires</th>
<th>Validity</th>
<th>Reliability</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D</td>
<td>0.80 with Health Utility Index Mark-3</td>
<td>0.70-0.85</td>
</tr>
<tr>
<td></td>
<td>0.70 with Short Form-6D (SF-6D)</td>
<td></td>
</tr>
<tr>
<td>CLDQ</td>
<td>discriminant validity in 150 Thai chronic</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>liver disease patients</td>
<td></td>
</tr>
<tr>
<td>WPAI</td>
<td>short-form health survey (SF-36)</td>
<td>0.71 to 0.87</td>
</tr>
</tbody>
</table>

Cronbach’s alpha of the EQ-5D and the CLDQ were 0.76, and 0.82, respectively.
Statistical methods for data analysis

- Quality of life by using EQ-5D: percent of patient reporting in some or severe health impairments (level 2+ level 3)
- Severity of liver disease by using CLDQ: mean (SD) scores
- Costs: Sum, Mean (SD) Baht/patient/year

- Factors effect to average CLDQ, EQ-5D VAS: *Multiple linear regression*
- Comparing frequency or mean scores within group among D0, M6 and M12: *Friedman K related test, Cochran’s Q*
- The statistical significant difference was defined as the *P* value less than 0.05.
Schematic of Medical and Economic Burden

**Medical Burden**

- **n:** D0 = 152, M6 = 140, M12 = 129

  - **Severity of Liver Diseases**
    - Chronic Liver Disease
  - **Questionnaire:** CLDQ

  - **Quality of Life**
    - EuroQol-5D: EQ-5D

**Economic Burden (n=129)**

- **Direct Medical Cost**
  - Radiology cost
  - Laboratory cost
  - ARV cost
  - Other medication excluded ARV
  - Each patient from HIS
  - Routine service cost
  - Capital cost
  - Out & In-patient Unit cost study of the hospital

- **Direct Non-medical Cost**
  - Transport expense
  - Food expense
  - Care giver expense
  - Extra health product expense
  - Patients' data

- **Indirect Cost**
  - Labor cost of work productivity loss
  - % Work impairment
  - Patients’ salary

  - Patients’ labor cost
  - Loss for hospital care
  - Out & In-patient
  - Patients’ data \( \times \) salary
### Baseline socio-demographic

<table>
<thead>
<tr>
<th>Parameters</th>
<th>$n$</th>
<th>Median (IQR) Mean (SD)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>152</td>
<td>39.0 (32.0-49.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>41.13 (11.56)</td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>152</td>
<td></td>
<td>83 (54.6)</td>
</tr>
<tr>
<td>Employee</td>
<td>152</td>
<td></td>
<td>105 (69.1)</td>
</tr>
<tr>
<td>Income, baht</td>
<td>152</td>
<td>10000.0 (7500.0-19625.0)</td>
<td>15,160.86 (29,264.36)</td>
</tr>
<tr>
<td>Had health security</td>
<td>152</td>
<td></td>
<td>141 (92.8)</td>
</tr>
<tr>
<td>ARV treatment</td>
<td>152</td>
<td></td>
<td>84 (55.3)</td>
</tr>
<tr>
<td>Months of treated ARV</td>
<td>84</td>
<td>21.0 (9.0-31.0) / 22.33 (18.03)</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>152</td>
<td></td>
<td>31 (20.4)</td>
</tr>
</tbody>
</table>

 calculations.

**Total loss = Death (3 cases) + loss follow up (20 cases)**

**Overall 152 pts**

**Total loss 7.9%**

**M6 140 pts**

**Total loss 15.1%**

**EQ-5D, CLDQ**

**M12 129 pts**

**Cost**
Baseline clinical characteristics

Treated ARV ($n=84$)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>$n$</th>
<th>Median (IQR)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Turcotte-Pugh (CTP) score of cirrhotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class A (Best; 5-6 points)</td>
<td>31</td>
<td></td>
<td>27 (87.1)</td>
</tr>
<tr>
<td>Class B (Moderate; 7-9 points)</td>
<td>31</td>
<td></td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>Class C (Worse; 10-15 points)</td>
<td>31</td>
<td></td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>HBeAg-negative</td>
<td>152</td>
<td></td>
<td>80 (52.6)</td>
</tr>
<tr>
<td>HBV DNA level, IU/ml</td>
<td>124</td>
<td>18.5 (10.0-16250.0)</td>
<td>&lt;2000</td>
</tr>
<tr>
<td>ALT/SGOT, U/l</td>
<td>152</td>
<td>27.0 (21.0-36.0)</td>
<td>8-40</td>
</tr>
<tr>
<td>AST/SGPT, U/l</td>
<td>152</td>
<td>26.0 (17.0-38.7)</td>
<td>5-35</td>
</tr>
<tr>
<td>Alkaline phosphates, U/l</td>
<td>149</td>
<td>68.0 (54.0-98.5)</td>
<td>15-112</td>
</tr>
<tr>
<td>Alpha-fetoprotein, ng/ml</td>
<td>136</td>
<td>2.2 (1.6-3.5)</td>
<td>0-14</td>
</tr>
<tr>
<td>Total bilirubin, mg/dl</td>
<td>152</td>
<td>0.6 (0.5-0.9)</td>
<td>0.5-1.0</td>
</tr>
<tr>
<td>Albumin, g%</td>
<td>152</td>
<td>4.3 (4.0-4.5)</td>
<td>3.5-5.0</td>
</tr>
<tr>
<td>INR</td>
<td>152</td>
<td>1.0 (0.9-1.1)</td>
<td>1.0-1.2</td>
</tr>
<tr>
<td>Hematocrit, mg%</td>
<td>152</td>
<td>39.0 (35.9-42.8)</td>
<td>37.0-54.0</td>
</tr>
</tbody>
</table>
Multiple linear regressions on QOL measured by using EQ-5D VAS, average CLDQ at D0\((n=152)\)

The R-squares of models with dependent variables EQ-5D VAS or CLDQM were 0.88 and 0.95, respectively.

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>95% CI</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EQ-5D VAS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Had health security</td>
<td>+75.23</td>
<td>39.29-111.17</td>
<td>0.001</td>
</tr>
<tr>
<td>Phase I immune tolerant</td>
<td>-49.50</td>
<td>-87.31 to -11.69</td>
<td>0.017</td>
</tr>
<tr>
<td>Month for CHB follow up &lt; 6</td>
<td>-47.12</td>
<td>-75.26 to -18.98</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>CLDQM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Had health security</td>
<td>+2.92</td>
<td>1.25-4.59</td>
<td>0.004</td>
</tr>
<tr>
<td>Month for CHB follow up &lt; 6</td>
<td>-1.49</td>
<td>-2.80 to -0.19</td>
<td>0.030</td>
</tr>
<tr>
<td>HCV co-infection</td>
<td>-1.47</td>
<td>-2.53 to -0.41</td>
<td>0.012</td>
</tr>
</tbody>
</table>
Comparison of mean (SD) CLDQ score within group among D0, M6, and M12 in each CLDQ domain

The lesser score means the more severity, the higher score means the less severity.

1 = All of the time, 2 = Most of the time; 3 = A good bit of the time; 4 = Some of the time;
5 = A little of the time; 6 = Hardly any of the time; 7 = None of the time

AB, Abdominal; FA, Fatigue; SY, Systematic symptom; AC, Activity; EM, Emotion; WO, Worry
Comparison of percent of patients reporting health impairment in each EQ-5D dimension of the presented and previous studies

<table>
<thead>
<tr>
<th>Authors, year, samples</th>
<th>Percent of patients reporting moderate or severe health problems</th>
<th>EQ-5D VAS (median (IQR/ mean (SD)))</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study, 2012, Thai CHB, OPD patient ( n=152 )</td>
<td>Mobility 13.2</td>
<td>Self care 3.9</td>
</tr>
<tr>
<td>EuroQol, 2004, 15 Countries, ( n=29,000 ), age 18-39 years</td>
<td>Mobility 5.5</td>
<td>Self care 2.0</td>
</tr>
<tr>
<td>- 40-59 years</td>
<td>Mobility 16.0</td>
<td>Self care 4.0</td>
</tr>
</tbody>
</table>

Median and mean age were 39 and 41 years.
### Economic Burden of CHB patients

Mean (SD) and sum of total cost, direct medical cost, direct non-medical cost and indirect cost in Thai Baht (n=129)

<table>
<thead>
<tr>
<th>Costs (Baht/year)</th>
<th>Mean (SD)</th>
<th>Sum (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cost</td>
<td>45,719.12</td>
<td>5,897,645.20</td>
</tr>
<tr>
<td></td>
<td>(64,647.43)</td>
<td>(100.0)</td>
</tr>
</tbody>
</table>

- **Direct medical cost**
  - Mean (SD): 32,115.04 (54,259.40)
  - Sum (%): 4,142,839.80 (70.25)

- **Direct non-medical cost**
  - Mean (SD): 4,539.17 (6,353.99)
  - Sum (%): 585,553.00 (9.93)

- **Indirect cost**
  - Mean (SD): 9,063.97 (19,068.75)
  - Sum (%): 1,169,252.40 (19.82)

### Comparison of mean (SD) annual direct medical cost (USD) of CHB of the presented and previous studies

<table>
<thead>
<tr>
<th>Author (published year), Country</th>
<th>Cost (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study, (2012), Thailand</td>
<td>1,048</td>
</tr>
<tr>
<td>Hu &amp; Chen (2009), China, Beijing</td>
<td>1636</td>
</tr>
<tr>
<td>Hu &amp; Chen (2009), China, Guangzhou</td>
<td>1452</td>
</tr>
<tr>
<td>Lu et al, (2013), China, Shandong</td>
<td>4552</td>
</tr>
</tbody>
</table>

It was the lower bound cost.

- Cost approach
- Local made drug
- Less severity patient
- Other health care were not obtained.
## Estimated economic burden of all CHB patients over Thailand

<table>
<thead>
<tr>
<th></th>
<th>Number of CHB patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2% prevalence</td>
</tr>
<tr>
<td>Number of Thai population</td>
<td>65,064,077</td>
</tr>
<tr>
<td>Prevalence of HBsAg</td>
<td>2.0-7.0%</td>
</tr>
<tr>
<td></td>
<td>1.3 million</td>
</tr>
<tr>
<td>One third develop to cirrhosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.4 million</td>
</tr>
<tr>
<td>Estimated new CHB case each year</td>
<td>8.6-10.4/100000</td>
</tr>
<tr>
<td></td>
<td>5,595</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD), Baht/pts/y</th>
<th>Sum (Million Baht/y)</th>
<th>Sum (Million Baht/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimate cost of all CHB over Thailand</td>
<td>45,719.12 (64,647.43)</td>
<td>59,493</td>
<td>208,227</td>
</tr>
<tr>
<td>Estimated cost for new CHB case each year (Baht)</td>
<td>45,719.12 (64,647.43)</td>
<td>255</td>
<td>310</td>
</tr>
</tbody>
</table>
LIMITATION

- Low severity patients
- ARV treated for 2-year
- Cost of outside the hospital was not included
- Information bias
CONCLUSION

Medical burden

• First study assessed both EQ-5D and CLDQ at over time.
• Variable significantly positively predict EQ-5D VAS was having health security ($B = 75.23$ (95% CI 39.29-111.17), $p=0.001$).
• CHB patient had physical and psychological impairments.

Severity of liver disease by using CLDQ
- At D0, the three domains with the least mean (SD) CLDQ scores were fatigue (5.05 (1.19)), systemic symptom (5.38 (1.16)), and worry (4.79 (1.24)).

Quality of life by using EQ-5D
- At D0, the most sequences of EQ-5D dimensions patients reporting moderate or severe problems were pain/comfort (54.6%) and anxiety (51.3%).
CONCLUSION

Economic Burden

• First time describes total cost of CHB patients including direct medical cost, direct non-medical cost, and indirect cost together with quality of life assessment.

• This is the lower bound cost or it is the cost of maintaining service for uncomplicated CHB.
  - Mean (SD) total cost was 45,719.12 (64,647.43) Baht/pt./year.
  - Direct medical cost of CHB patients was quite low with 1,048 USD/patient/year (32,115.04 Baht, 30.63 Baht = 1 USD).

• CHB incurs a large magnitude economic burden in Thailand.
  - Mean (SD) total cost was 45,719.12 (64,647.43) Baht/pt./year.
  - Estimated economic burden of all CHB patients over Thailand ranged 59-208 billion Baht/year.
BENEFIT OF THE STUDY

For clinical practice setting

- Psychological burden effects to CHB patients.
- QOL could reflect sign and symptom of CHB patients.
- Regular liver biomarker monitoring could reduce anxiety.
- New information of the medical and economic burden of Thai CHB patients in the same population
- Medical burden: Quality of life determined affect of the disease on patients’ life via patients’ perspective.
THANK YOU