THE SOCIOECONOMIC IMPACT OF HEPATITIS E IN NEPAL

KATHRYN L. CLARK, RENE M. HOWELL, ROBERT M. SCOTT, DAVID W. VAUGHN, MRIGENDRA P. SHRESTHA, CHARLES F. LONGER, AND BRUCE L. INNIS

Division of Preventive Medicine, and Department of Virus Diseases, Walter Reed Army Institute of Research, Washington, District of Columbia; Division of Infectious Diseases, The Johns Hopkins University, Baltimore, Maryland; Department of Virology, Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand

Abstract. Hepatitis E disease is responsible for substantial morbidity in Nepal. A socioeconomic analysis was performed to describe the costs and the effects of hepatitis E disease (HE) on health status in a Nepalese population living in the Kathmandu Valley. A modified health status index was used to quantify healthy days lost associated with HE. One hundred thirty-four individuals recently recovered from HE were interviewed in June 1998. The median age was 22 years and 60% were female. Study participants were sick and bedridden for a median of 22 and 10 days, respectively. The median healthy days lost per individual was 35 (768,000 total per region). The median cost of illness per individual, including direct and indirect, was $37 ($1,238,676 total per region). The percentage of yearly income lost for wage earners totaled 19.4%. Hepatitis E disease is associated with significant costs and loss of healthy days in Nepal. Further research is warranted to understand and limit this common disease.

Viral hepatitis represents an important public health concern in Nepal, where hepatitis E virus (HEV) infection causes most of the hospitalized acute hepatitis disease in Kathmandu and the surrounding area. Hepatitis E disease (HE), formerly known as enterically transmitted non-A, non-B hepatitis, primarily afflicts populations in countries with poor environmental sanitation. This disease is similar to hepatitis A disease (HA) with respect to transmission, clinical course, and absence of chronic disease. Hepatitis E disease attack rates are highest in young adults rather than in children as is the case with HA. However, there can be greater morbidity associated with HE and the mortality rate of HE is higher than that found with HA in certain subsets of the population. The incidence of fulminant hepatitis and the mortality rate for HE are highest among pregnant women in their third trimester. Age-specific infection rates for persons 12–19 years of age have been estimated at 99/1,000 during sporadic transmission and higher during outbreaks. Use of immune serum globulin as prophylaxis does not provide protection. No vaccines are currently available.

Hepatitis E disease impacts individual health across three dimensions: increased morbidity (or mortality), increased real and self-perceived disability, and increased direct and indirect expenditures. This study provides a descriptive analysis of a set of individuals with HE in Nepal and describes the socioeconomic impacts of HE through quantification of the health (morbidity and disability) and economic effects on diseased individuals across these three dimensions.

METHODS

Individuals included in the socioeconomic analysis were recruited from transmission studies of HEV in pregnant women, families, and outbreaks in both rural and urban settings. These transmission studies were conducted by the Walter Reed Army Institute of Research (Department of Virus Diseases), the Armed Forces Research Institute of Medical Sciences (AFRIMS), and their field laboratory in Kathmandu (Walter Reed/AFRIMS Research Unit, Nepal). From the transmission studies, 134 cases of clinical hepatitis in 131 families were identified from surveillance based at the Patan, Ayuvedic, and Teku Infectious Diseases Hospitals, and from private practices in the Kathmandu Valley. Acute HE was defined as 1) signs or symptoms of acute liver injury (with elevated alanine aminotransferase levels if acute-phase serum was available), 2) virologic or serologic evidence of acute HEV infection, and 3) confinement at home for at least 2 days because of disease severity. Individuals who died of HE, primarily pregnant women, were excluded from the analysis. A household was defined as a group of individuals sharing a specific kitchen unit.

Demographics, disability days, and expenditure data were collected by four trained community health workers in Nepalese using face-to-face structured interviews conducted during June 1998. Given a long duration of morbidity associated with HE and the study time frame, individuals were questioned an average of 356 days after illness with a range of 106–728 days. Disability information with regard to bed-days, the ability to perform occupation, other work roles, and think clearly was collected in a Likert scale format (normal, below normal, much below normal, and very much below normal).

Measurement of the ability of the individual to perform daily tasks was used as a means to quantify the non-mandatory socioeconomic impact of temporary morbidity, defined as median days of healthy life lost. To arrive at the days of healthy life lost, disability data were adjusted using an index developed by the World Health Organization (WHO). In this index, disability ratings were assigned according to self-reported capabilities in three areas: ability to work, strength, and ability to think. These are similar to the WHO disability classifications of occupation, recreation, recreation, and education. The disability index is described in Table 1. Days of healthy life lost were calculated for each individual by multiplying the WHO disability rating by the corresponding number of days associated with each level of functioning. For example, an individual out of work and bedridden for 4 days (4 × 0.81), would receive a healthy days lost score of 3.24 for those 4 days. Total days of healthy life lost were aggregated to provide an estimate of total healthy days lost for the interviewed population as a whole. Median values and 95% confidence intervals are reported.

Monetary expenditures and lost wage data were collected in self-reported open format questions. Alternative healers...
included faith healers, as well as Buddhist and Ayurvedic practitioners. Direct health care expenditures included outpatient care (including alternative practitioners), hospitalization, medications (including prescription, as well as fruits and glucose), and travel to locations to receive medical care. Population median expenditures were calculated for those individuals who reported each expenditure. Indirect costs included lost wages (defined as income lost because of inability to work and decreased income because of decreased production while working), and payment for replacement workers or assistance with housework and child care. The equation used to calculate total costs follows the formula: [(daily wage \times number days unable to work) + (income lost while working because not working normally) + (fees paid by the individual for outpatient care, healers, hospitalization, medicine, and travel) + (payment for replacement workers or assistance for housework and child care)].

It was assumed that no one received paid sick leave and that no type of health insurance was available. Cost of illness was obtained from the patient perspective.

A pilot questionnaire was administered to 62 individuals. A revised questionnaire clarifying several questions was developed. This revised questionnaire was administered by the same four interviewers as the original. Before administration of the revised questionnaire, the interviewers were formally retrained using written tests and role playing.

Twenty-three of the 62 individuals who completed the pilot questionnaire were available for questioning using the revised version. The remaining 39 individuals from the pilot study were unavailable for readministration of the questionnaire. Reported days not worked for the 23 individuals completing both questionnaires was used to assess reliability of individual responses with regard to recall using the Pearson correlation coefficient. As a result of the pilot analysis, many other variables were significantly altered on the revised questionnaire and were not appropriate for comparison. The correlation coefficient for reported days not worked was 0.7, implying reasonable consistency of recall for this variable. The analysis reported in this manuscript describes data obtained from the revised questionnaire only.

The study protocol was approved by the Nepal Health Research Council and the Walter Reed Army Institute of Research Human Use Review Committee. Informed consent was obtained from all study subjects before administering the questionnaire. All ages were treated equally in the disability index.

### RESULTS

Of the 134 individuals responding to the revised questionnaire, 30 individuals acted as a proxy respondent to answer questions for another individual (primarily mothers responding for dependent children). Sixty percent of the participating individuals were female and the median age was 25 years (range = 5–65). The median age in the male participants was 19 years (range = 5–54). Twenty-six individuals were less than 18 years of age. Sixty-one percent (82 of 134) of all participants were married, 94% of whom lived in self-owned homes. Of the 80 participating females, 33% (26 of 80) were pregnant during their illness. A median of six individuals resided in each household. Sixty-nine percent (92 of 134) of participating individuals were supported by someone else.

Thirty percent (40 of 134) of participants were students, 26 of whom were less than 18 years of age and did not report an occupation. These 26 individuals were excluded from the adult and occupation-related parameters. The remaining 14 students (18 years of age or older) are included in the adult and occupation related parameters due to their adult age and earning potential. Consequently, there were 108 individuals included in the adult and occupation-related parameters.

Fifty-six percent (61 of 108) were homemakers, 28 of whom also performed other tasks such as farming and wool spinning; 16% (17 of 108) were farmers (38% [41 of 108] when including homemakers who also farmed). The remaining 28% (30 of 108) of the adults reported diverse occupations such as photographer and bricklayer. The term workers in the remainder of the manuscript refers to the 65 individuals listing an occupation, excluding homemakers with no other occupation (33), and students with no other occupation (36). The 62% (40 of 65) of the workers reporting earning a monetary wage will be referred to as wage earners throughout the manuscript. The 25 individuals who reported an occupation without reporting earned monetary wages may
Table 2
Number of morbidity days and adjusted disability days per individual, n = 134

<table>
<thead>
<tr>
<th>Days</th>
<th>Number of days, median</th>
<th>Disability adjusted healthy days lost, median (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedridden</td>
<td>10†</td>
<td>8.1 (5.8, 12.0)</td>
</tr>
<tr>
<td>Sick but not bedridden</td>
<td>7†</td>
<td>4.2 (1.2, 6.0)</td>
</tr>
<tr>
<td>Not sick but with residual disability</td>
<td>351</td>
<td>14.7 (0, 26.2)</td>
</tr>
<tr>
<td>Overall</td>
<td>378</td>
<td>35 (29.2, 38.6)</td>
</tr>
</tbody>
</table>

*CI = confidence interval.
† Since medians were used, the numbers are not additive and cannot be used to determine overall median sick days.

Morbidity and disability. Overall, individuals were bedridden for a median of 10 days (95% confidence interval [CI] = 7–15) and sick for a median of 22 days (95% CI = 15–30). Workers and homemakers could not work for a median of 26 days (95% CI = 15–30). Monetary wage earners could not work for a median of 30 days (95% CI = 19–42). Of those reporting weight loss, the median weight loss was 4 kg (95% CI = 4–5). Ten percent (8 of 82) of those married reported that their spouse became sick with a similar illness. Fourteen percent (19 of 134) said that children in the household had a similar illness, and 22% (29 of 134) reported another household member with a similar illness.

Disability in terms of healthy days lost for time spent in bed was a median of 8.1 days (95% CI = 5.8–12.0). For time sick, but not bedridden, the median healthy days lost was 4.2 (95% CI = 1.2–6). After recovery, residual disability in terms of ability to work, strength, and ability to think was a median of 14.7 healthy days lost (95% CI = 0–26.2). The median total disability per individual (which included disability while bedridden, sick but not bedridden, and residual disability) was 35.0 healthy days lost (95% CI = 29.2–38.6) or 93 days lost/1,000 potential healthy days (i.e., 9.3% of potential healthy days from the date of illness onset to date of questionnaire administration). The total healthy days lost from HE in this population was 4,444, or 87 days to date of questionnaire administration. The total healthy days lost from HE in this population was 4,444, or 87 days to date of questionnaire administration.

Costs. Diverse forms of medical attention were sought by the population under study (Table 3). Forty-six percent (61 of 134) visited an outpatient doctor or nurse during their illness. The median total expenditures for outpatient doctor or nurse services was $9 (95% CI = 5–18) per individual and a total of $772 was expended by the participants as a whole.

Sixty-three percent (85 of 134) visited an alternative healer. The median total expenditures for alternative healer was $8 (95% CI = 5–11) per individual and a total of $895 was expended by the participants as a whole.

Seventeen percent (23 of 134) were hospitalized. The median total expenditure for hospitalization was $45 (95% CI = 30–85) per individual and a total of $1,364 was expended by the participants as a whole.

Eleven percent (15 of 134) took medicine other than that prescribed by the nurse, doctor, alternative healer, or that received in the hospital. The median total expenditure for additional medicine was $6 (95% CI = 3–9) per individual and a total of $28 was expended by the participants as a whole.

Eight percent (11 of 134) traveled to remote locations to receive care. The median total expenditure for transportation was $1 (95% CI < 1–6) per individual and a total of $17 was expended by the participants as a whole.

Eighty-one percent (108 of 134) made payments for dietary supplements (primarily fruits and glucose) in addition to those listed above, paying a median of $9 (95% CI = 8–14). A total of $1,660 was expended by the participants as a whole for these additional expenses.

Overall, for total direct cost of illness, participants paid a median of $21 (95% CI = 16–25) for a total of $4,735 (Table 3). Wage earners spent a median of 6.4% (95% CI = 4.8–9.8) of their estimated yearly monetary income on their direct medical costs.

Indirect costs from illness include lost wages and expenditures for help with house work and replacement workers and are in addition to the direct costs of illness described.

Table 3
Median direct costs ($) associated with hepatitis E disease, n = 134*

<table>
<thead>
<tr>
<th>Main category</th>
<th>No. (%)</th>
<th>Service fee</th>
<th>Medicine costs</th>
<th>Test costs</th>
<th>Transportation costs</th>
<th>All subcategories (median)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient</td>
<td>61 (46)</td>
<td>&lt;$1</td>
<td>$6</td>
<td>$3</td>
<td>$2</td>
<td>$9</td>
</tr>
<tr>
<td>Alternative healer</td>
<td>85 (63)</td>
<td>&lt;$1</td>
<td>$8</td>
<td>$5</td>
<td>$2</td>
<td>$8</td>
</tr>
<tr>
<td>Hospital</td>
<td>23 (17)</td>
<td>$32</td>
<td>$48</td>
<td>$10</td>
<td>$3</td>
<td>$45</td>
</tr>
<tr>
<td>Medicine</td>
<td>15 (11)</td>
<td>–</td>
<td>$5</td>
<td>–</td>
<td>$1</td>
<td>$6</td>
</tr>
<tr>
<td>Travel‡</td>
<td>11 (8)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>$1</td>
<td>$1</td>
</tr>
<tr>
<td>Dietary</td>
<td>108 (81)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>$9</td>
</tr>
<tr>
<td>Overall</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>$21</td>
</tr>
</tbody>
</table>

* = not applicable.
† Median of total direct costs for each individual across each main cost category.
‡ Travel = travel to distant place to recover, includes lodging.
Table 4
Median indirect cost ($) associated with hepatitis E disease, n = 134*

<table>
<thead>
<tr>
<th>Main category</th>
<th>No. (%)</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unable to work</td>
<td>26 (19)</td>
<td>$28</td>
</tr>
<tr>
<td>Worked below normal production level</td>
<td>10 (7)</td>
<td>$5</td>
</tr>
<tr>
<td>Substitute worker</td>
<td>20 (15)</td>
<td>$46</td>
</tr>
<tr>
<td>Overall</td>
<td>--</td>
<td>$46</td>
</tr>
</tbody>
</table>

* = not applicable.

above. Fifty-two percent (34 of 65) of workers had occupations where their income was dependent on their level of production. Forty percent (26 of 65), all of whom were monetary wage earners, earned lower wages while sick because they could not work. Among wage earners, a median of $38 (95% CI = 33–46) was lost per individual because of decreased income for days unable to work resulting in a total of $1,213 lost wages for the participants as a whole. Fifteen percent (10 of 65) of wage earners earned lower wages (monetary or other) while sick and working due to decreased production as a result of not working at full capacity. A median of $15 (95% CI = 3–44) was lost per individual because of decreased income on days unable to work normally resulting in $178 total lost wages for the wage earners, representing a median of 6.9% (95% CI = 0–13.1) of their yearly income.

Seventy-eight percent (76 of 98) of workers and homemakers had someone work in their absence. Twenty-six percent (20 of 76) of them paid someone else a total median of $46 (95% CI 23–48) to work in their place for a total of $786 for all participants.

Fifty-five percent (59 of 108) of adults (age ≥ 18 years old) reported usually being the primary caregiver to children. Fifty-eight percent (34 of 59) of them could not care for children while ill. Ninety-one percent (31 of 34) had childcare provided, but only 1 paid for this help ($3). Of the 66% (72 of 108) of adults normally caring for the house (cleaning, cooking), 86% (62 of 72) were unable to do so during their illness. Eighty-two percent (59 of 72) had someone else care for the house during their illness; however, only one person paid for these services ($ < 1). Twelve percent (16 of 134) of all individuals reported that their family had less food while they were ill.

A total of 37 individuals with any indirect costs paid a median of $46 (95% CI = 35–81) for a total of $2,181 for indirect costs paid by the population (Table 4).

Median total cost of illness (direct and indirect) for 128 individuals was $37 (95% CI = 23–45). Six individuals had no expenditures or lost wages. Percentage of yearly income lost for wage earners for their cost of illness totaled 19.4% (95% CI = 15.7–22.8).

**DISCUSSION**

Hepatitis E disease is associated with significant disease costs and disability in Nepal. Individuals interviewed were sick for a median of 22 days and were bedridden for a median of 10 days. The 65 workers could not work for a median of 26 days. Median disability in days of healthy life lost was 93 per 1,000 days. While ill, the study population paid a median of $37 in total costs and the wage earners lost a median of almost 20% of their annual income in lost wages and direct cost of illness. Even though the median individual total indirect cost was more than the median total direct cost, most of the indirect costs pertained to monetary wage earners only. With regard to direct costs, the cost of hospitalization was the highest individual median direct cost expended; however it only applied to 17% of the respondents and accounted for 29% of the direct total cost. Dietary supplements applied to 81% of individuals consuming 35% of the direct total cost.

Although dramatic, these results most likely underestimate the socioeconomic impact of HE in Nepal. Percentage of income spent on cost of illness was under-represented because wage earners within each family may have paid for the costs of illness for the whole family, and not just those associated with their own illness. Workers not reporting a monetary wage may earn income in terms of other goods and services, so their illness may represent a burden that is not financial and may have been missed in this analysis. Although decreased non-monetary income is difficult to quantify and was not considered in this analysis, it deserves consideration as a significant impact of HE. Bartering and debts to family and friends were not included (for example, the need to reimburse a sister who watched the patient’s children for several days during the illness). Additionally, absence from work has implications beyond associated loss of wages. For example, the inability to farm during planting or harvest may lead to financial loss after the individual has recovered from HE. Money spent on transportation for health care and products did not include costs of wear and tear on any self-owned vehicles. Pain and suffering experiences, such as worrying about having enough food for the children, were either not fully assessed or not fully incorporated into lost wages or physical disability ratings. Any residual disability after the date the questionnaire was administered was not captured.

Our method of determining the socioeconomic impact on individuals did not consider how much people would have been willing to pay to avoid contracting the disease, but rather estimated expenditures and lost income associated with HE that could be used for other means had they not been ill with HE (opportunity costs).

Few analyses similar to that reported here have been conducted in developing countries. This kind of questionnaire is difficult to construct in a developing, heterogeneous country with a currency that is not exclusively monetary. Despite the difficulties, development of such an instrument is important. It may be used in the future in conjunction with the WHO disability rating system to quantify socioeconomic burden of diseases and for comparisons to determine public health priorities.

There are several limitations to the generalizability of our results. Because only individuals with illness severe enough to confine them to rest at home for at least 2 days qualified as subjects, our ability to capture data on individuals with mild illness was limited. Some were fatal cases among the pregnant women cohort at the hospital from which many volunteers were recruited, and they were not considered for enrollment. Individuals included in this study were recruited and do not represent a random sample of the population. Expanded studies including random selection and control...
populations are necessary to more rigorously analyze the impact of HE in a more generalizable population. Thus, results from this analysis may distort the true population values.

Days of healthy life lost figured in the total temporary disability, which did not fully consider the marginal disability (for example, a person may have stayed in bed 6 of the 12 reported bedridden days for another reason). From an individual perspective, total impact was appropriate because of the limited amount of leisure time in this population.

Data were collected an average of 356 days after illness. This duration was necessary due to the long duration of illness in many individuals and limited time frame of study. This duration may inhibit recall of illness and cost data. Receipts and employment records were reviewed when available to strengthen the confidence in reliability of recall. However, recall remains a threat especially in underdeveloped countries where resources for confirmation of self-reported data are scarce. Nonetheless, the results were similar across individuals, indicating general trends.

In India and other developing countries, more than half of the acute viral hepatitis in young adults is due to HEV infection. Outbreaks have been reported involving 29,300 and 79,000 individuals in India. The Xinjiang HE epidemic in China involved 120,000 individuals. Hepatitis E virus was the reported etiology of an outbreak involving at least 300 persons in Vietnam in 1994. Hepatitis E disease outbreaks have also been reported among the militaries of Nepal and Ethiopia. Prevention and control efforts directed against this geographically widespread problem have the potential to prevent significant morbidity, substantial expenditures for health care, and lost wages in countries other than Nepal. Total costs to the individual with HE would be expected to exceed those reported for this population in higher income brackets also at risk for HE.

Although not a random sample, the individuals recruited and interviewed for this analysis represent a heterogeneous sample of the Kathmandu Valley. Hepatitis E disease rates in the Kathmandu Valley have been estimated to be 20/1,000 person-years. The estimated total burden of HE in the Kathmandu Valley for 1 year would be more than $1,238,676 U.S. and 32 healthy days lost for each of the estimated 24,000 individuals with HE, totaling 768,000 days (based on our results extrapolated to population estimates of 1.2 million from the Kathmandu Municipal City Office). This estimate may overestimate the impact of disease in individuals only mildly affected. However, it does not include disease that resulted in death.

A vaccine, in conjunction with increased provisions for clean drinking water, offers hope for preventing the protracted morbidity from this infection for which there is no specific, curative treatment. Eventually, by using the results presented here along with incidence data and information on probable infrastructure improvements or vaccine costs, effectiveness, and side effects, a formal cost-benefit analysis evaluating prevention strategies (water treatment, vaccination programs) could be conducted. Women of child-bearing age and young refugees in camps, as well as people from industrialized countries visiting endemic areas, would greatly benefit from prevention activities to protect against HE.

The results of this study illustrate the large burden of HE. The morbidity, disability, as well as the direct and indirect costs associated with HE in Nepal are substantial. Research is warranted to avert the extensive consequences and morbidity associated with this disease. This study should be viewed as an initial examination and should prompt further efforts into this area of research where information is lacking.

Acknowledgments: We thank Chandra Rai, Kusum Bajracharya, Anandi Vaidya, and Bishnu K. Shrestha for careful structured interviews; volunteers; Dr. Sanjaya K. Shrestha for medical support; Scott Gigliotti, Pranee Saisang, Prachaktra Panthushri, and Surin Sirirond for specimen processing; Dr. Khin Say Aye Myint, Choompun Manomuth, Duangrat Mongkolsirichaikul, Nawarat Charensri, Patama Monkhongdee, and Kittinun Hussem for HEV serology; Dr. Boonyos Raengsakulrach, Sumita Narupiti, and Chonticha Klungthong for the HEV reverse transcription–polymerase chain reaction; Tipawan Kungvanrattana for database management; and the Nepal Health Research Council for endorsement of research studies of hepatitis E.

Financial support: This study was supported in part by a cooperative research and development agreement with SmithKline Beecham Biologics (Rixensart, Belgium).

Authors’ addresses: Kathryn L. Clark, Division of Preventive Medicine, Walter Reed Army Institute of Research, Washington, DC 20307-5100. Rene M. Howell, Division of Infectious Diseases, The Johns Hopkins University, Baltimore, MD 21205. Robert M. Scott and Mrigendra P. Shrestha, Department of Virology, Armed Forces Research Institute of Medical Sciences, Bankok, Thailand. David W. Vaughn and Bruce L. Innes, Department of Virus Diseases, Walter Reed Army Institute of Research, Washington, DC 20307-5100. Charles F. Longer, Department of Medicine, University of Tennessee College of Medicine, 975 East Third Street, Box 96, Chattanooga, TN 37403.

Reprint requests: David W. Vaughn, Department of Virus Diseases, Walter Reed Army Institute of Research, Washington, DC 20307-5100.

REFERENCES


