HEPATITIS C AMONG CHILD TRANSFUSION AND ADULT RENAL DIALYSIS PATIENTS IN INDONESIA

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Abstract. Hepatitis C virus (HCV) prevalence among high-risk pediatric and adult patients was evaluated. The study included 269 adults and 150 children in a case-control research design. Risk factors of HCV exposure in Indonesia were assessed among adult renal dialysis patients and pediatric patients who received multiple blood transfusions. A high prevalence of anti-HCV was found among the adult renal dialysis patients, measured by second-generation immunoenzymoassay tests. Family members of dialysis patients, who served as a comparison group for dialysis patients, were found to have a 9.0% seroprevalence. The prevalence of anti-HCV among pediatric patients with hematological disorders was found to be 39.0%. The comparison group seroprevalence (pediatric patients and family members) was 4.3% among sera available for confirmatory testing. Patients with history of hospitalization (odds ratio [OR] = 7.94, 95% confidence interval [CI]: 4.06–15.51, P = 0.0001), blood transfusion (OR = 6.85, 95% CI: 3.95–11.88, P = 0.0001), circumcision (OR = 2.39, 95% CI: 1.43–3.99, P = 0.0001), or marital partner/family member history of jaundice (OR = 3.62, 95% CI: 1.97–6.62, P = 0.0001) were found to have an increased odds of HCV exposure compared with individuals without similar histories.

INTRODUCTION

Hepatitis C virus (HCV), a causative agent in acute hepatitis, has been found to be associated with chronic disease and increased risk of liver cancer. Hepatitis C virus, referred to as parentally transmitted non-A, non-B hepatitis (NANB), has been reported to be the most common transfusion-associated hepatitis in many countries worldwide. Clinical symptoms of HCV are similar to acute hepatitis associated with hepatitis B virus (HBV). However, HCV infection has been characterized by longer incubation times; chronic, persistent infections; and a sevenfold increased risk of hepatocellular carcinoma. More than 2% of healthy blood donors (152/7,252) were found to have serological evidence of exposure to HCV in a broadly representative serosurvey in Indonesia. This epidemiological study evaluated clinical findings from pediatric patients who received multiple blood transfusions and renal dialysis patients to assess the prevalence and risk factors of HCV in Indonesia.

MATERIALS AND METHODS

Study sample. The study population included 173 high-risk patients (98 dialysis patients, 75 hematology patients) and 246 individuals for a comparison group (96 spouses, 75 nonhematology patients, 75 parent caregivers; 217 females and 202 males; Table 1). Patients were recruited from one of two hospitals in Jakarta, Indonesia, including Gatot Subroto Army Hospital and Cipto Mangunkusumo Hospital. The case-control prevalence study targeted poly-transfused pediatric patients involving 75 high-risk hematology patients compared with hospitalized, nonhematology pediatric patients. Serological testing was also completed among parent caregivers of the high-risk pediatric patients. Ninety-eight adult renal dialysis patients were evaluated; their spouses served as a comparison group. Study participants were interviewed to collect information about their clinical history. Sera were examined for anti-HCV as evidence of a history of HCV infection. The pediatric and adult participants in this high-risk-comparison research design study, ranged in age from 1–13 years (mean = 8.0 years) and 14–79 years (mean = 42.2 years), respectively.

One hundred adult renal dialysis patients were initially recruited for the study from Gatot Subroto Army Hospital between January 1994 and October 1994, 98 of whom consented to participate in the study (see Table 1). This first subgroup included 98 adult (aged 14–79 years) renal dialysis patients and 96 spouses (n = 194). These family members formed the comparison group and had no history of hepatitis, dialysis, or prior transfusions.

Pediatric patients were recruited for the study from the Cipto Mangunkusumo Hospital. This second subgroup included 75 children (aged 1–13 years) with hematological disorders and 75 pediatric patients hospitalized for nonhematology related illnesses (aged 5–13 years) enrolled between November 1995 and May 1996. The comparison group consisted of pediatric outpatients and hospitalized children with no history of jaundice or transfusions (n = 150). The high-risk pediatric patients were matched by age and gender to hospitalized nonhematology pediatric patients within the comparison group. Health and HCV serostatus information was also gathered from 75 parent caregivers (aged 15–49 years).

The comparison groups, including spouses of renal dialysis patients and hospitalized pediatric patients, were selected on the basis of their similarity to the high-risk groups. The individuals comprising the hospital-based comparison group for the polytransfused pediatric patients were specifically identified and matched by age and gender, because the two groups differ only in their history of receipt of blood transfusion products. Parent caregivers of high-risk pediatric patients were evaluated primarily to examine the potential HCV transmission within the family.

Serological testing. Patient and comparison group sera were screened by an enzyme-linked immunosorbed assay (HCV ELISA, Abbott Laboratories) test at U.S. NAMRU-2 in Jakarta. Confirmatory testing was completed on sera found to be reactive with an immunoblot assay (HCV Immunoblot, Genelabs Diagnostics) by an independent laboratory, RIBA-2 Chiron Company, in Singapore. A questionnaire gathering demographic and risk-related information was ad-
ministered to each high-risk comparison patient or family member by a trained interviewer. A questionnaire was completed with information about personal history of hospitalization, receipt of blood products, circumcision, kerokan, acupuncture, and family history of jaundice. Responses to the questionnaire and laboratory test results were analyzed using SPSS statistical software (SPSS, Inc.).

**Statistical analysis.** The purpose of the evaluation was to examine the association between the detection of anti-HCV antibodies and clinical characteristics of renal dialysis patients and pediatric patients compared with the comparison group. The descriptive analysis included frequencies, t-tests, chi-square analyses, and Fisher’s exact test, as appropriate. Logistic regression statistical models were used to evaluate the association between five health-related and eight socioeconomic, family health, and lifestyle factors with the dichotomous (yes or no) outcome variable, anti-HCV serology results.

Health-related factors selected from the questionnaire included hospitalization, surgery, blood transfusion, history of jaundice, and positive serology for hepatitis B antigen. Demographic and lifestyle factors examined included age, gender, history of breast-feeding, circumcision, family member history of jaundice, ear piercing, acupuncture, and practice of kerokan. The renal dialysis and hematology patients were considered the high-risk group for HCV. All hematology patients had blood dyscrasias, including hemophilia, thalassemia, acute leukemia, and hypoplastic or autoimmune anemia.

The odds ratio (OR) reported for each univariate logistic regression model indicated the strength of association between the disease state and the clinical, familial, or lifestyle characteristic and was reported as an increased or reduced odds of having the disease state. An odds ratio was classified as statistically significant if the p value was less than 0.05 when the OR confidence interval (95% CI) did not include 1. Results include some odds ratios that did not reach statistical significance, because these statistics serve to enhance our understanding of the epidemiology of HCV infection.

**RESULTS**

A high prevalence of anti-HCV 63.4% (59/93) was found among renal dialysis patients. Renal dialysis patient spouses were found to have a 9.0% (8/90) seroprevalence among the sera available for HCV confirmatory testing. The prevalence of anti-HCV among polytransfused pediatric patients with hematological disorders was found to be 39% (29/75). The seroprevalence among the hospitalized pediatric comparison group was 4.5% (3/67), whereas 4.2% (3/72) of the parent caregivers had detectable anti-HCV.

Spousal pairs were examined among renal dialysis patients. Although the difference did not reach statistical significance ($\chi^2 > 0.5, 1$ df), twice as many spouses (8/90; 9.0%) of renal dialysis patients within the comparison group had anti-HCV antibodies than individuals in the comparison group for high-risk hematology patients (3/72; 4.2%). There was an association between the length of marriage and anti-HCV positivity among spouses of renal dialysis patients ($r = -2.29, P = 0.024$); however, many other factors, including age and gender, also increase risk of HCV exposure.

Responses to a health-related questionnaire were evaluated using logistic regression models testing the combined adult and pediatric data set. Univariate logistic models with socio-demographic variables representing age and gender (coded as 0 [female] or 1 [male]) were found to be significantly related to the presence of anti-HCV. However, age was not found to contribute significantly to a multivariate logistic model in the presence of the gender variable, when age was represented by a dichotomized variable representing higher risk after 14 years (OR = 1.523, 95% CI 0.929–2.498, $P = 0.095$). Males were found to have an increased odds of having anti-HCV (OR = 2.107, 95% CI 1.32–3.34, $P = 0.002$). The regression analysis results are reported after adjustment for gender. Results are reported as the odds ratio of a positive serological test for anti-HCV.

Eight nonhematology pediatric patients and three parent caregivers were lost to follow-up because they had been discharged or were unavailable for blood sample collection. Two spouses were unavailable for blood sample collection. A total of 22 (of 419, or 5.3%) sera samples were unavailable for confirmatory HCV serological testing, including 5 (of 98) from renal dialysis patients, 6 (of 96) from renal dialysis patient spouses, 8 (of 75) from the pediatric comparison group, and 3 (of 75) from parent caregivers of pediatric hematology patients.

Results indicated that people with a history of hospitalization (OR = 7.940, 95% CI 4.063–15.518, $P = 0.0001$), surgery (OR = 5.903, 95% CI 3.572–9.756, $P = 0.0001$), or receipt of any blood product or transfusion (OR = 6.856, 95% CI 3.956–11.882, $P = 0.0001$) were significantly ($P < 0.05$) more

**Table 1**

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk groups</th>
<th>Sample size</th>
<th>Population enrollment</th>
<th>Seroprevalence % of anti-HCV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk comparison group study</td>
<td>Renal dialysis patients</td>
<td>184 adults: 96 patient-spousal pairs, 2 patients without spouse, (aged 14–79)</td>
<td>Adult (&gt; 14 yr) patients recruited from Gatot Subroto Army Hospital, Jakarta, Indonesia</td>
<td>63.4% high-risk group</td>
</tr>
<tr>
<td></td>
<td>Polytransfused pediatric patients</td>
<td>150 children: 75 hematology patients (aged 1–13 yr) matched by age/gender with 75 hospitalized nonhematology patients (aged 5–13 yr); and 75 parent caregivers (aged 15–49 yr)</td>
<td>Children (1–13 yr) with hematological disorders from Cipto Mangunkusumo Hospital, Jakarta, Indonesia</td>
<td>9.0% comparison group</td>
</tr>
</tbody>
</table>

* Antibody to hepatitis C virus.
Hepatitis C in Indonesia

likely to have detectable anti-HCV than the comparison group, which was negative for anti-HCV (Table 2). Individuals with a history of jaundice (OR = 3.753, 95% CI 2.008–7.017, \( P = 0.0001 \)) and family history of jaundice (OR = 3.621, 95% CI 1.978–6.627, \( P = 0.0001 \)) were significantly (\( P < 0.05 \)) more likely to have detectable anti-HCV than the comparison group. Circumcision among males (OR = 2.494, 95% CI 1.290–4.822, \( P = 0.007 \)) and females (OR = 2.25, 95% CI 1.006–5.055, \( P = 0.048 \)) was found to be a risk factor for HCV exposure. A detectable difference was found when considering ear piercing, kerokan, and acupuncture (OR = 1.838, 95% CI 0.972–3.474, \( P = 0.061 \)) in a comparison of the adult and pediatric populations, although the result did not reach statistical significance.

DISCUSSION

This study includes clinical characteristics that may serve as guidelines for intervention measures to reduce exposure to HCV. The high seroprevalence of anti-HCV among the two hospital-based populations examined in this study serves to confirm the strong relationship of HCV with posttransfusion hepatitis previously reported in the literature. Of concern is the fact that the relatively low prevalence of HCV among healthy blood donors (2.1%) and the adult comparison group (4.0%) cannot explain the risk of exposure to HCV associated with blood transfusions in Indonesia. Other studies completed within Southeast Asia reported high seroprevalence (10–15%) among special population groups, including posttransfusion hepatitis patients and polytransfused pediatric patients (Soeprapto and others, unpublished data).

Hepatitis transmission from individuals with acute hepatitis to family members has been the focus of many epidemiological studies. Among spouses of renal dialysis patients in this study, the seroprevalence (9%) was found to be higher than the polytransfused pediatric study comparison group (4.2%) and other Indonesian adult population groups (1–3%). This lends support to HCV transmission between heterosexual partners. This study demonstrated a significant association between length of marriage and evidence of HCV exposure among spouses of renal dialysis patients. There was a strong association between family history of jaundice and patient anti-HCV positivity. Serological findings from adult caregivers of hematology patients were found to more commonly have positive results for anti-HCV (4.2%) compared with healthy blood donors (2.1% anti-HCV positive) in Indonesia.

Anti-HCV was found to be more common with increasing age, indicating that adjustment for age should be included in risk of HCV exposure assessments. Among pediatric patients examined, younger children (<5 years) had lower seroprevalence (38.5% = 5/13) than children older than 10 years (61.3% = 19/31). An association between the number of blood transfusions received, which would be greater among older patients, was also documented among the pediatric study population. The study provides strong evidence that HCV exposure among the high-risk groups was related to the receipt of blood transfusions, pooled blood products, and contaminated dialysis equipment. In a study of acute episodes of NANB among polytransfused thalassemic children in Italy, high rates of chronic disease were found to be related to multiple reinfections during transfusions.

Participation with ritual ceremonies or folk remedies that

### TABLE 2

Summary of risk-related factors associated with hepatitis C virus exposure

<table>
<thead>
<tr>
<th>Risk of HCV exposure</th>
<th>High risk ((n = 160)) (%)</th>
<th>Low-risk comparison ((n = 229)) (%)</th>
<th>Odds Ratio (OR)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health-related history factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>159 (91.6)</td>
<td>88 (36.1)</td>
<td>7.940†</td>
<td>4.063–15.518</td>
</tr>
<tr>
<td>Surgery</td>
<td>80 (46.7)</td>
<td>33 (13.9)</td>
<td>5.903†</td>
<td>3.572–9.756</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>80 (49.1)</td>
<td>3 (1.3)</td>
<td>6.856‡</td>
<td>3.957–11.882</td>
</tr>
<tr>
<td>History of jaundice</td>
<td>42 (24.4)</td>
<td>8 (3.4)</td>
<td>3.753†</td>
<td>2.008–7.017</td>
</tr>
<tr>
<td>HB Ag positive</td>
<td>12 (7.1)</td>
<td>13 (5.5)</td>
<td>ns</td>
<td>–</td>
</tr>
<tr>
<td>Anti-HCV positive‡</td>
<td>88 (52.4)</td>
<td>14 (6.1)</td>
<td>ns</td>
<td>–</td>
</tr>
<tr>
<td><strong>Demographic/lifestyle factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>116 (60.1)</td>
<td>77 (39.9)</td>
<td>2.107‡</td>
<td>1.322–3.343</td>
</tr>
<tr>
<td>Female</td>
<td>57 (26.3)</td>
<td>160 (73.7)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Average age (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children</td>
<td>8.0 yr (1–13)</td>
<td>7.6 yr (1–13)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Adults</td>
<td>46.6 yr (14–79)</td>
<td>39.5 yr (14–72)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Breast-feeding (n = 90 children)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>32 (24.5)</td>
<td>68 (75.5)</td>
<td>ns (1.900)</td>
<td>0.750–4.750</td>
</tr>
<tr>
<td>Female</td>
<td>115 (46.0)</td>
<td>135 (54.0)</td>
<td>2.397</td>
<td>1.437–3.997</td>
</tr>
<tr>
<td>Family history of jaundice</td>
<td>32 (18.7)</td>
<td>24 (10.1)</td>
<td>3.621†</td>
<td>1.978–6.627</td>
</tr>
<tr>
<td>Any piercing/kerokan/</td>
<td>95 (54.9)</td>
<td>172 (72.6)</td>
<td>ns (1.838)</td>
<td>0.972–3.474</td>
</tr>
</tbody>
</table>

HCV = hepatitis C virus; ns = nonsignificant; HB Ag = hepatitis B antigen.

† Comparison group included 75 pediatric nonhematology patients and 75 primary family member care givers related to the pediatric patients and 96 spouses of renal dialysis patients with no evidence of hepatitis.

‡ Univariate logistic regression models predicting patient positively to anti-HCV.

§ Kerokan is a custom that involves the scraping of the skin with a coin.
involve cutting or scratching of the skin, as with circumcision and kerokan, has been reported to be associated with increased risk of HCV exposure. In a study of a tribal group in Central India, where the practice of folk remedies was common, there was a high seroprevalence of HCV. In the current study, detectable difference was found when considering ear piercing, kerokan (custom of scraping skin with a coin), and acupuncture in the comparison of adult and pediatric populations. People reporting hospitalization, surgery, or transfusion also had elevated odds of HCV exposure compared with individuals without these risk factors. This study had a limited scope because it focused only on two high-risk populations. Further research on the epidemiology of HCV related to HCV potential exposure and transmission is needed. The purpose of this research was to identify specific risk factors in acquiring hepatitis C exposure, alerting clinicians to the possibility of risk factors for hepatitis infection other than blood transfusion or contamination of dialysis equipment.

This research offers evidence that limiting specific health practices and risk factors may reduce the risk of hepatitis C exposure. Blood products and dialysis equipment cannot successfully be used as life-saving remedies if HCV contamination allows the spread of this debilitating, chronic disease. Health care providers should institute an epidemiological safety net by instituting sensitive serological screening among patients at high risk of HCV exposure. Current research related to coinfection of HCV and HIV may provide opportunities for screening among representative sample populations in the future.

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