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A Clinical Profile of Hepatitis A Patients in Jakarta, Indonesia

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Abstract

Background: To determine the incidence of hepatitis A infections and the clinical profiles of adult patients admitted to public hospitals in Jakarta, Indonesia. **Methods:** This was a cross-sectional study that utilised consecutive secondary data from internal medicine wards of seven public hospitals in Jakarta between 2011 and 2013. Eligibility criteria included patients over the age of 18 years and an ICD-10 diagnosis code of B15, acute hepatitis A. Case proportion was reported per 1000 people by dividing incidence per year to total in-ward patients. Clinical profiles were reported descriptively. Laboratory results were compared and categorised into groups of patients aged below and above 25 years old. **Results:** Data revealed that hospitalisations of patients with hepatitis A had decreased from 2011 to 2013. 289 patients were studied, the majority were young adults (18-25 years old) and their common chief complaints were nausea (36%), fever (24%), and jaundice (21%). Higher bilirubin levels were seen in older patients. There were 13 patients coinfected with hepatitis B, one patient coinfected with hepatitis C, and one patient coinfected with HIV. **Conclusions:** The proportion of hepatitis A infection amongst adults admitted to public hospitals in Jakarta was low and had decreased during the study period. Most of the patients reported classical clinical manifestations. This study found that the targeted age group may benefit from receiving routine hepatitis A vaccinations.

Keywords: epidemiology, Hepatitis A, Indonesia, vaccination

Introduction

Hepatitis A is an acute liver disease caused by the hepatitis A virus (HAV), a ribonucleic acid picornavirus. The HAV is transmitted through the faecal-oral route, either from person to person or through contaminated food or water. It is strongly related to personal hygiene and lower standards of living.[1,2] In the last few years, many developing countries with a high endemicity of hepatitis A infections have reported a decreased incidence of the disease. These findings were related to improvements in standards of living, sanitation, and socio-economic conditions.[3] Between 1978 and 1981 Indonesia reported 98% seroprevalence of HAV in persons aged 15 to 19 years old. A comparison of data from 1994 to 1996 showed that among children aged 10 to 19 years there was 97% seroprevalence of HAV in those living in rural areas versus only 35% seroprevalence in 15 to 19 year olds residing in urban areas.[4] Urban populations experience a higher incidence of adult patients with symptomatic HAV which can increase mortality and morbidity rates.[4,5] These conditions have encouraged many Asian countries to reassess and reevaluate their hepatitis A vaccination policies.

In Indonesia the HAV infection occurs mostly in children.[4] 30% of children aged below 6 are infected by the HAV and usually develop non-specific symptoms or are asymptomatic. However, adults infected with the HAV will develop more classic symptoms such as jaundice and whilst the majority of cases do not require hospitalisation, disease severity will increase with a

patient's age.[6] Hospitalisation rates can be used as an indicator for disease severity and can affect a patient's productivity, social and economical outcome.[7] There is no specific treatment available for hepatitis A that can shorten the duration of illness.[6,8] Indonesia experiences a moderate degree of endemicity for the HAV and currently has no recommendations for routine vaccinations.[3] Limited data is available regarding hepatitis A prevalence in Indonesia and as such, this study aims to determine the proportion of hepatitis A infection, establish a clinical profile, and provide a comparison of disease severity between age groups that were admitted to public hospitals in Jakarta between 2011 and 2013.

Methods

This cross-sectional study was carried out in seven public hospitals in Jakarta, which represent each district of Jakarta using a convenience sampling methods. These hospitals were Cipto Mangunkusumo Hospital (Central Jakarta), Gatot Soebroto Central Army Hospital (Central Jakarta), Fatmawati Hospital (South Jakarta), Cengkareng Hospital (West Jakarta), Anak Bunda Harapan Kita Hospital (West Jakarta), Sulianti Saroso Hospital (North Jakarta), and Persahabatan Hospital (East Jakarta). All data was collected consecutively from each patient's medical records. Ethical approval was obtained from the Ethical Board of the Universitas Indonesia.

Study subjects. Medical records of all patients older than 18 years, who tested positive to the IgM anti-HAV, were reviewed. Clinical information obtained from these medical records was used to answer a structured questionnaire, including information about sex, age, length of hospitalisation, symptoms, and the onset of disease. Data on laboratory results such as AST, ALT, total bilirubin, and direct bilirubin levels at admission, as well as CD4 cell counts and IgM anti-HAV, HbsAg, anti-HCV, and HIV status were recorded.

Statistical analysis. The WHO's classification for demographic, social, and related economic data was used to compare our the age groups.[9] Additionally, possible relationships between hepatitis A disease severity and increasing age were explored. Independent sample T-tests and Mann-Whitney tests were used to determine differences between the two groups. Statistical analysis was carried out using the Statistical Program for Social Sciences (v 20.0; SPSS Inc., Chicago, IL, USA). The two-tailed value of $p < 0.05$ was considered statistically significant.

Results

Between 2011 and 2013 there was a total of 289 cases of laboratory confirmed, acute hepatitis A admitted to 7 public hospitals in Jakarta. To break this down further, there were 105 confirmed cases in 2011, 117 cases in 2012, and 67 cases in 2013.

Table 1. Clinical Characteristics of Patients with Acute Hepatitis a who were admitted to 7 Public Hospitals in Jakarta between 2011 and 2013

Variables	2011 (n = 105)	2012 (n = 117)	2013 (n = 67)
Total in-ward patients	16,868	23,571	21,991
Rates of Hospitalisation	6.22/1000[#]	4.96/1000	3.04/1000
Median age, (IQR)	24 (9)	25 (10)	26 (14)
Male (%)	73 (69.5)	75 (64.1)	35 (52.2)
Median onset, days (IQR)	4 (4)	4 (4)	5 (4)
Median length of stay, days, (IQR)	6 (4.75)	6 (5)	7 (3)
Hepatitis B (%)			
Positive	6 (5.7)	3 (2.6)	4 (5.9)
Negative	78 (74.3)	77 (65.8)	49 (73.1)
Not Tested	21 (20)	37 (31.6)	14 (21)
Hepatitis C (%)			
Positive	1 (1.0)	0 (0.0)	0 (0.0)
Negative	66 (62.9)	72 (61.5)	44 (65.7)
Not tested	38 (36.2)	45 (38.5)	23 (34.3)
HIV (%)			
Positive	0 (0.0)	1 (0.9)	0 (0.0)
Not tested	105 (100)	116 (99.1)	67 (100)
Lab findings, median (IQR)			
AST (U/L)	546 (725)	566 (838)	342 (629)
ALT (U/L)	1,083.5 (963)	1,192 (1202)	768 (976)
Total Bilirubin (mg/dL)	5.8 (4.1)[*]	6.2 (4.0)[**]	6.7 (8.3)[***]
Direct Bilirubin (mg/dL)	4.3 (3.5)[*]	4.7 (3.6)[**]	5.4 (5.9)[***]

[#]No data available from Gatot Soebroto Central Army Hospital in 2011
*Data valid for 93 subjects
** Data valid for 102 subjects
*** Data valid for 60 subjects

Among 217 patients with a positive IgM anti-HAV whom screened for Hepatitis B, we found 13 patients tested positive to HbsAg, thus the rate of hepatitis B coinfection was 4.5%. Additionally, 183 patients with positive IgM anti-HAV were screened for hepatitic C, and only 1 patient tested positive (0.3%). None of the patients in the study sample tested positive for a triple infection. Only 1 patient was HIV seropositive with a CD4 level of 789/µL, and was being treated with antiretrovirals. There were no cases of hepatitis leading to death included in this study.

The median age of the sample population was 25 years and the ratio of male to female subjects was 1.7:1. The most commonly affected age group was those aged 18 to 25 years (n = 162), followed by the 25 to 35 years age group (n = 78), the 36 to 45 years age group (n = 32), the 46 to 55 years age group (n = 13), and finally patients over 55 years (n = 4).

The demographics and laboratory findings of all 289 subjects is summarised in Table 1.

The most common chief complaint of all 289 hospitalised subjects was nausea (36%), followed by fever (24%), and jaundice (21%). A summary of symptoms as reported by patients is shown in Figure 1.

Comparison of laboratory parameters, using the Mann-Whitney test, between patients aged below and above 25 years showed that there was a significant difference for direct bilirubin, 4.5 mg/dL versus 5.4 mg/dL ($p < 0.05$), and total bilirubin, 5.8 mg/dL versus 6.8 mg/dL ($p < 0.05$) respectively. There was no significant differences between other parameters such as AST, ALT, and indirect bilirubin (Table 2 & 3).

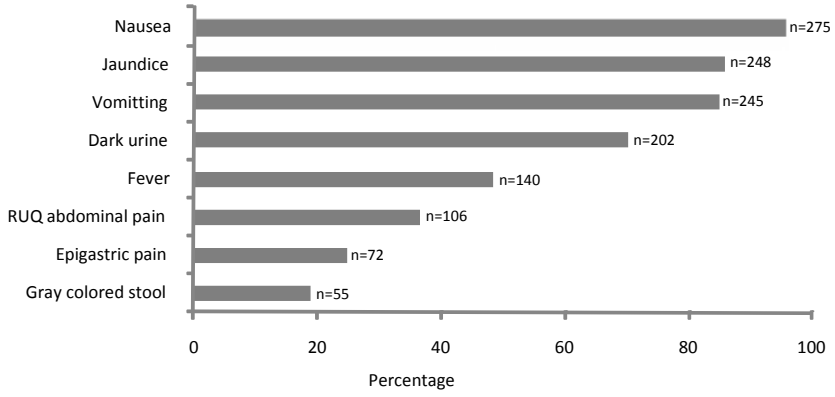

Figure 1. Common Symptoms Experienced by Patients with Acute Hepatitis A (n = 289). RUQ: Right Upper Quadrant

Table 2. Comparison of AST and ALT Values Between Two Age Groups

Variable	Age < 25 yo (n = 140)	Age ≥ 25 yo (n = 146)	*p* value
	Median (IQR)	Median (IQR)	
AST	536 U/L (698.0)	476 U/L (763.5)	0.836
ALT	1,039 U/L (1008.5)	1,012 U/L (1242.3)	0.943

Table 3. Comparison of Bilirubin Levels between Two Age Groups

Variable	Age < 25 y.o. (n = 123)	Age ≥ 25 y.o. (n = 132)	*p* value
	Median (IQR)	Median (IQR)	
Direct Bilirubin	4.5 mg/dL (3.1)	5.4 mg/dL (5.6)	0.029
Indirect Bilirubin	1.3 mg/dL (0.8)	1.4 mg/dL (1.7)	0.545
Total Bilirubin	5.8 mg/dL (3.6)	6.8 mg/dL (6.4)	0.032

Discussion

National reports include acute hepatitis A as a leading cause of hospitalisation in Indonesia (39.8-68.3%), however the incidence of infection has steadily decreased in the last 3 years, in the 7 public hospitals in Jakarta that were studied.[8] This finding is in contrast with a report from Korea's Centre for Disease Control and Prevention, which showed an exponentially increasing number of symptomatic HAV infections since 2006.[10] However, a recent report from the United States of America showed similar findings of decreased hospitalisation rates, from 0.72 cases per 100,000 to 0.29 cases per 100,000.[7] Declining incidence rates of hepatitis A in many developing countries has lead to a changing level of endemicity.[3] Indonesia's close neighbour, Singapore, has also seen a significant reduction in the incidence of hepatitis A from 1.8 cases per 100,000 in 1989 to 0.7 per 100,000 in 2009.[1] As such, the decreased incidence of acute hepatitis A in 7 of Jakarta's public hospitals in the past three years is not sufficient to determine the endemicity status of the country, and data on the sero-prevalence of anti-IgG HAV in all age groups are needed.

Patients with acute hepatitis are not routinely screened for complete seromarkers of hepatitis due to the costs involved. This study found very few cases of coinfection with other hepatitis or blood borne viruses. A report from North India (2011-2012) showed that among 267 hepatitis virus cases, there were 34 cases of hepatitis coinfection with 6 cases of HAV-HBV coinfection.[11] Similarly, no routine tests were conducted to determine HIV status amongst patients with acute hepatitis. A study in Poland in 2008 to 2009, found that out of 40 homosexual patients with the HAV, 6 patients were positive for HIV.[12] Patients with HIV have a higher risk of contracting the HAV due to high risk behaviours such as practicing male to male anal sex, and higher incidences have also been reported amongst men in Europe who identify as an injecting drug user or homosexual.[12,13] Generally speaking, the ratio of hepatitis A cases between men and women is 1.7:1.[1,6] Limited information on subject's history of intravenous drug use was collected during this study.

There is a wide spectrum of clinical manifestations of hepatitis A, from asymptomatic to fulminant. The severity of hepatitis A depends on the age of the person and symptoms typically include malaise, anorexia, abdominal discomfort, vomiting, fatigue, diarrhea, and less commonly fever, headaches, arthralgia, and myalgia. The classic manifestations are elevated levels of liver enzymes, the appearance of dark urine, dark-coloured stools, and jaundice.[14] These clinical manifestations are due to the host immunologic response against the viral infection, which can induce acute liver injury. Intrahepatic inflammation impairs transport of conjugated bilirubin, leading to an accumulation of bilirubin in the skin and sclera, which causes jaundice.[15] The most common presenting symptoms found in this study were nausea (36%), followed by fever (24%), and jaundice (21%).

The majority of subjects in this study (56%) were aged between 18 and 25 years old, this age group is predominantly consisted of workers or students presented with the classical features of acute hepatitis A infection. Hepatitis A does not usually result in long-term complications in this age group, however it can cause disadvantage to their productivity, social circles, and the economy. The average length of hospitalisation in the sample group was 6 days and there are no specific therapies available to shorten the length of illness.[8] The only effective prevention of hepatitis A is via vaccination, with the vaccine having a 94-95% protective efficacy and predicted protection up to 45 years.[14] Vaccination has been proven effective at maintaining a lower risk of infection as per studies conducted on toddlers in Israel.[16] Therefore, WHO recommends that vaccines should be administered universally in low endemic countries like America, Australia, and Northern and Western Europe. Additionally, they advise that should be targeted to people in high risk groups, such as men who have sex with men, tourists travelling to highly endemic countries, those requiring life-long treatments with blood products, people living in hepatitis A outbreak communities, people who are at a high risk of contracting infections, or those with chronic liver disease. WHO recommends national vaccination programs for children older than 1 year old, based on the changes in the incidence of acute hepatitis A, changes in endemicity from high to intermediate, and the vaccines cost effectiveness.[14]

Results from our laboratory testing showed a marked increase of ALT compared to AST and elevated levels of direct bilirubin, these are similar to the results of other studies.[17] Lee *et al*. found the mean levels of ALT was 3108 U/L in Korean people with acute Hepatitis A, which is higher than the mean levels of ALT found in our study population. This difference may be due to the older age distribution of the Korean sample group.[18] As per the United Nations recommendations, the sample population was divided into two groups based on the median age, for ease of classification.[9] Our results also found that levels of total bilirubin and direct bilirubin were significantly higher in the over 25 age group. Higher levels of bilirubin in patients aged over 25 reflects that the hepatitis A virus tends to be more symptomatic in older patients. Differences of transaminase levels between the two age groups failed to show any significant impact.

Hepatitis A vaccination is not currently mandatory in Indonesia; however certain countries in Asia are considering universal hepatitis A vaccinations. This

study is representative of the current prevalence of Hepatitis A in Jakarta. With the capital of Indonesia being an important destination for both work and tourism in Asia, further research regarding the national seroprevalence to determine endemicity levels and the cost effectiveness of providing routine hepatitis A vaccines are needed.

Conclusions

Low hospitalisation rates of patients with the hepatitis A infection in Jakarta was represented by young productive age. Routine Hepatitis A vaccinations in young adults, as a part of the national immunisation program, is beneficial as it is highly protective, it increases productivity by reducing absenteeism from work, and decreases the health cost of hepatitis A in Indonesia.

Conflict of Interest Statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

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