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Use of risk scores for screening of hepatitis C of blood donors in remote areas

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Hepatitis C virus (HCV) infection is considered as an emerging health problem in Myanmar. Seropositivity rates vary from 3% in blood donors at major blood banks in Yangon to over 10% in northeast and northwest border areas. Determination of HCV is limited in remote areas as it is expensive and some test systems need special equipment. To assist in the control of hepatitis C in Myanmar, we developed a simple system for screening of HCV infection using risk scores. The scores were based on the data obtained from HCV surveys carried out at the northeast and northwest border areas of Myanmar. The database consisted of 652 subjects (250 males, 402 females), aged 18 years to 60 years. Multivariate analyses revealed the following factors to be related to HCV infection in the subjects: more than 30 years of age, Odd Ratios (OR)=2.41 (p=0.001); a history of tattooing, OR= 1.78 (p=0.035); a history of hepatitis in the family, OR=1.58 (p=0.049). The screening scores for HCV infection were developed using risk scores. Validity was analyzed using the Receiver Operating Characteristics curve. The sensitivity of the system was 80% and the specificity 37% when a cut-off score of $\geq$2.5 was used. By increasing the cut-off score, higher specificity (up to 80%) could be achieved at the cost of decreasing sensitivity. The developed risk scores could be applied for screening of blood donors for HCV infection in areas where laboratory HCV testing could not be performed.

INTRODUCTION

Hepatitis C virus (HCV) infection is an important health problem in many countries [1]. HCV was shown to be the major causative agent of non-A, non-B hepatitis and that it is associated with blood transfusion. Although the acute infection is usually asymptomatic and may not be recognized clinically, the subsequent chronic infection is usually life-long and may lead to chronic liver disease leading to liver cirrhosis and hepatocellular carcinoma. In fact it had been proven in Japan as a single most important aetiological factor for the development of hepatocellular carcinoma, where the incidence of hepatitis B virus infection is low [2].

HCV is regarded as an emerging health problem in Myanmar. Reports in early 90's demonstrate HCV infection in one third of patients with hepatocellular carcinoma [3], and in 2.5% of apparently healthy subjects [4]. In recent years, the Myanmar-Japan cooperation study group observed that 2 cases were positive for anti-HCV (5.9% positivity rate) among 34 voluntary blood donors [5]. During May 2000 to Oct 2002, a total of 102,632 donors were screened and the overall anti-HCV positivity rate was

found to be 2.84% [6]. The prevalence of antibody to hepatitis C virus (anti-HCV) was found to be 2.8% among 569 subjects (246 males, 323 females), aged 3 months to 74 years, residing at Mayangone Township, Yangon Division [7]. A recent study showed a higher prevalence of HCV among the population in a northeast border town than blood donors and community in Yangon [8].

For the control of HCV infection in Myanmar, screening for HCV infection is essential. We carried out this study to devise a risk screening form for HCV infection for use in remote border areas where HCV testing is not easily available.

MATERIALS AND METHODS

Cross-sectional, community-based studies were carried out during 2002 and 2003 in northeast and northwest border townships of Myanmar. The northeast border (Muse Township) study population comprised of 349 subjects (137 males, 212 females) aged 12 months to 70 years. Tamu Township (northwestern border) survey included 502 persons (aged 1year to 65 years). During the surveys, consecutive samples were collected from subjects residing at the above mentioned areas. Those who refused consent were excluded from the study. A standardized proforma was used to collect biological and sociodemographic data. Clinical and family histories were carefully asked and recorded. Special emphasis on history of jaundice, history of jaundice in family members, history of dental and surgical operations, and blood transfusion history were noted. From each subject, two milliliters of blood was collected under aseptic measures and sera separated. Sera were transported back to the National Blood Research Centre of the Department of Medical Research (LM) and stored at -80ºC till further analyses. Ortho-HCV Ab PA test II (Orth-Clinical Diagnostics, Fujiredbio Inc., Tokyo, Japan) was used for determination of seropositivity to HCV. These two data bases were combined and those with ages qualified for blood donation were further selected as the data base for the present study. The data base consists of 652 subjects (250 males, 402 females), aged 18 years to 60 years residing at Muse and Tamu Townships.

Statistical methods

Data analysis was performed with SPSS (Statistical Package for Social Scientists Ver 10.1; SPSS Corporation, Chicago, IL, U.S.A.) on a IBM computer. Univariate and bivariate tests were carried out to determine differences between groups. Differences were considered significant if $p < 0.05$. The associated factors were further analysed using odds ratio and multiple logistic regression analysis [9].

RESULTS

General characteristics

Of the 652 subjects, 250 were males and 402 were females. Their ages ranged from 18 years to 60 years with a mean (SD) age of 34.53 (10.9) years. Twenty- five percent of the study population (45%) has achieved high school and university status. Bamars constituted 60% of the study population and the remainder was ethnic groups including Shans, Chins, and Kachins.

HCV antibody prevalence

One hundred and four subjects were found to be seropositive to hepatitis C infection (15.9%). Males had a higher prevalence of anti-HCV seropositivity than females (18.8% vs 14.2%; Student's 't' test, $p=0.12$). No significant difference in age was found between males and females (35.36 ± 11.5 vs 34.02 ± 10.4, $p=0.13$). The anti-HCV seropositivity rate significantly increased with increasing age group. It was found to be the lowest (9.4%) in 18-20 years age group and highest (24.1%) in the 51-60 years age group. Anti HCV seropositivity in 21-30 years, 31-40 years and 41-50 year age groups were found to be 10%, 18.3% and 21.1% respectively.

Associated risk factors for anti-HCV seropositivity

After univariate analysis, it was found that the significant associated factors among the population were: (a) age 30 years and above, (b) presence of tattoos, (c) history of jaundice in the family.

Table 1. Associated factors for anti -HCV sero-positivity by univariate analysis

Associated factors	Anti-HCV seropositivity			Remarks
	No. of tested	No. of positive	Percentage	
Gender				
Male	250	47	18.6	p=0.117
Female	402	57	14.2	
Education group				
Primary & below	271	49	18.1	p=0.418
Secondary & above	327	51	15.6	
Marital status				
Never	265	38	14.3	p=0.339
Ever	367	63	17.2	
Family size				
6 members & below	432	67	15.5	p=0.614
More than 6 members	217	37	17.1	
History of liver diseases				
Yes	139	26	18.7	p=0.317
No	513	78	15.2	
History of transfusion				
Yes	52	8	15.4	p=0.907
No	600	96	16	
History of tooth extraction				
Yes	271	41	15.3	p=0.619
No	380	63	16.6	
History of surgery				
Yes	210	33	15.7	p=0.891
No	440	71	16.1	
History of ear piercing				
Yes	302	45	14.9	p=0.486
No	349	59	16.9	
History of tattooing				
Yes	101	23	22.7	p=0.043
No	550	81	14.7	
History of hepatitis in the family				
Yes	176	35	19.9	p=0.047
No	475	69	14.5	
Age 30 years & above				
Yes	388	78	20.1	p=0.001
No	264	26	9.8	

There was no significant association with gender, education, marital status, and size of the family, history of liver diseases, and history of transfusion, history of tooth extraction, history of surgery, and history of ear piercing (Table 1).

Multiple logistic regression was applied for controlling confounders and for evaluating the effects of associated factors on HCV infection in the studied group. After analysis, 3 variables: age of more than 30 years, Odd Ratios (OR) =2.41 (p=0.001); a history of tattooing, OR= 1.78 (p=0.035); a history of hepatitis in the family, OR=1.58 (p=0.049) were found to have effect on HCV infection (Table 2).

Table 2. Associated factors for anti-HCV sero-positivity among the studied population by multivariate analysis

Associated factors	Adjusted OR	95% CI of OR	p value
Age 30 years & above			
Yes	2.41	1.49 - 3.90	p=0.001
No	1		
History of tattooing			
Yes	1.78	1.05 - 3.03	p=0.033
No	1		
History of hepatitis in the family			
Yes	1.58	1.00 – 2.51	p=0.049
No	1		

Development of a simple risk screening form for screening of HCV infection using risk scores

The risk screening form for HCV infection was developed by using scores from Table 2 as follows: risk score = scores of age 30 years and above plus a history of tattooing plus history of hepatitis in the family. Score of age 30 years and above = 2.5, score of a history of tattooing = 2, score of family history of hepatitis = 1.5. The calculation of risk scores was analyzed and the validity of this model for predicting the risk of HCV infection was calculated by Receiver Operating Characteristics curve (ROC curve). The

sensitivity of this model was 82% and the specificity was 39% when the cut-off score of ≥ 2. If the cut-off score was increased to ≥ 4, the specificity increased to 80% but the sensitivity was greatly reduced to 40%. The optimal cut-off score was determined by the ROC curve (Fig. 1) and was found to be ≥ 2.5, with a sensitivity of 80% and a specificity of 37%. A risk screening form for HCV infection in population aged 18 to 60 years is proposed in Fig. 2.

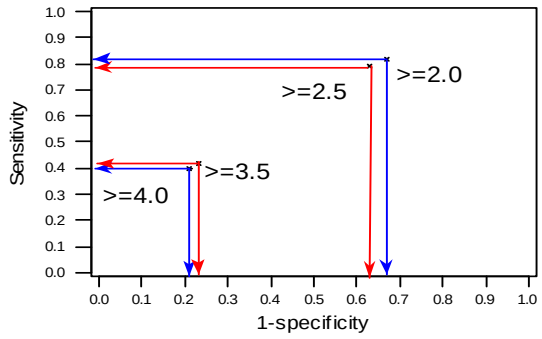

Fig. 1. ROC curve for prediction of HCV infection

Risk screening form for HCV infection among blood donors in remote areas (*where HCV screening is not possible*)			
Name		Age	Years
Gender Male/Female		Marital status	
Residence			
Risk factors	Status	Full scores	Check list scores
Age 30 years & above	Yes	2.5	
	No	0	
History of tattooing	Yes	2	
	No	0	
History of hepatitis in the family	Yes	1.5	
	No	0	
	Total	6	
Interpretation	Total check list scores ≥ 2.5 indicates the risk for HCV infection at the sensitivity of 80%. Please do not allow blood transfusion unless confirmed to be negative by HCV serological test.		

Fig. 2. Risk screening form for HCV screening among blood donors in remote areas

DISCUSSION

The problem of hepatitis C infection in Myanmar is well recognized and efforts to control it in the blood donor population have been initiated since the year 2000. With the support of Japan International Cooperation Agency under the Control of hepatitis C in Myanmar project, hepatitis C screening of 154161 blood donors during May 2000 to April 2004 had demonstrated the prevalence of HCV infection to be 2.6% in Myanmar blood donors [10]. Data from Europe demonstrated lower than 1% HCV seropositivity in blood donors [2], and 1-2% of blood donors were found to be HCV seropositive in the Far East [11]. However, high rates of HCV infection had been reported with 4% of the blood donors being positive for anti-HCV antibodies in Egypt with higher prevalence rate of 15% in the rural areas of the country [12].

We have studied the HCV prevalence among 349 subjects (137 males, 212 females) aged 12 months to 70 years residing at the Muse Township, Northern Shan State. The overall prevalence of anti-HCV postivity was found to be 13.5% [13]. In northwestern border towns, Tamu and Kalay, a field survey carried out during 2003 revealed that 12.7% of the study population of 502 persons (aged 1 year to 65 years) to be anti-HCV seropositive [14]. Although HCV prevalence surveys could not be considered to be representative of the population at large, it could be concluded that significant higher rates of HCV infection exists among apparently healthy populations residing in border areas.

A study carried out in Yangon blood donors had also outlined similar associated factors. Higher prevalence of anti-HCV positivity was found in those with history of surgical operation, tooth extraction, ear piercing and tattooing. The seropositivity increases with age. In addition, education levels and previous history of blood transfusion had been regarded as possible associated factors [7, 15].

HCV screening tests are expensive and are not easily available in all parts of Myanmar, especially remote areas. The developed risk

screening form will be very helpful in such situations. The screening form is cost free and could be easily used by a medical person, in charge of blood collection. The facts are also in consistent with those mentioned in the donor self deferral form but the proposed form is very simple and could be handled by a person with a little medical knowledge.

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