Risk factors for hepatitis C virus infection among blood donors in an HIV-epidemic area in Thailand

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Abstract

***Objective* – The role of sexual transmission in hepatitis C virus (HCV) infection has not yet been completely elucidated. This study aimed to compare the risk factors for HCV and human immunodeficiency virus (HIV) infection in an HIV epidemic area of Thailand where HIV is mainly transmitted heterosexually.**

***Design and subjects* – Sera from 3053 blood donors were collected and tested for HCV and HIV between January and March 1994. Altogether 1756 (57·5%) of the donors were interviewed about demographics and several risk factors.**

***Results* – The prevalence rates of HIV and HCV infections determined by antibody assays were 2·3% and 2·2%, respectively. Sexual risk factors were clearly shown among anti-HIV positive donors. These clear associations were not found, however, among anti-HCV positive donors. In contrast, previous histories of injecting drug use and being tattooed were found in some anti-HCV positive donors but less frequently in anti-HIV positive donors.**

***Conclusions* – Sexual transmission may play a relatively minor role in HCV transmission compared with HIV, in this area.**

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Hepatitis C virus (HCV) is responsible for most cases of non-A non-B hepatitis that arise after blood transfusion. Many blood service establishments have begun testing for antibody to the virus. The prevalence rate of anti-HCV positivity among blood donors in Thailand was reported to be 1–2%.[1-2] The role of parenteral transmission in HCV infection (for example, via blood transfusion, injecting drug use, and being tattooed) was well documented. Although some studies suggested that sexual transmission has a role,[3-6] this has not yet been fully established. This study aimed to compare risk factors for anti-HCV positivity among blood donors with those for antibody to human immunodeficiency virus (HIV). Since this study took place in an HIV epidemic area, where most HIV transmission is heterosexually driven, the comparison may provide information on the role of sexual transmission of HCV.

The study was conducted in a province in northern Thailand which covers an area of about 4000 square miles with a population of 1·2 million in 1993. The first case of acquired immunodeficiency syndrome (AIDS) in this province was a female commercial sex worker (CSW) with symptoms of chronic diarrhoea and wasting in 1984. The first AIDS case was reported in Bangkok in the same year. This suggested that the epidemic of HIV/AIDS in this province started approximately at the same time as in Bangkok and much earlier than in other parts of the country. A national serological survey performed in June 1994 showed the following rates of HIV infection among various high risk groups in this province: injecting drug users, 21%; brothel based female CSW, 49%; non-brothel based CSW, 16%; male clients of sexually transmitted disease (STD) clinics, 25%; women attending antenatal clinics of the provincial hospital, 6%; and blood donors, 2·3%. The provincial hospital where this work was performed is a 720 bed hospital with about 12 000 blood donations per year. Approximately half of the donations took place in the blood bank of this hospital and the rest at remote donation sites. On site donations were run solely by the hospital staff but donations at remote sites were a result of the cooperative activities of the staff of the hospital, the provincial branch of Thai Red Cross Society, and district hospitals. One or two mobile donations were organised weekly. About 50–300 donors attended each mobile donation site.

Methods

Between January and March 1994, sera of all blood donations (on site and mobile) were stored and tested for anti-HCV antibody. Anti-HCV testing was done at the laboratory of Hepatitis Virus Section of Thailand's Virus Research Institute. A solid phase enzyme immunoassay for detecting antibody to HCV core antigen in human serum or plasma was used. The HCV core antigen used in this assay was prepared by expression of HCV cDNA coding amino acids 1–115 in *Escherichia coli* (B strain).[7-8] Sera that reacted to one test were retested. Only repeatedly (twice) reactive sera were considered positive. Based on our previous experience with the test,[9] no confirmatory testing was necessary.

During the same period, donors who donated blood at the office of the hospital blood bank during office hours (9.00 am to 5.00 pm) were invited to join the study. After informed consent, donors were interviewed about demo-

Table 1 Prevalence of anti-HIV and anti-HCV positivity in relation to the characteristics of blood donors, January–March 1994

Variables	*Anti-HIV*		*Anti-HCV*	
	Positive (%)	*Negative*	*Positive (%)*	*Negative*
Age				
≤35 y	56 (3·48)	1552	35 (2·18)	1573
>35 y	14 (0·97)	1431	31 (2·15)	1414
	p<0·001		p=0·953	
Sex				
Male	62 (2·72)	2217	48 (2·11)	2231
Female	8 (1·04)	866	18 (2·33)	856
	p=0·002		p=0·935	
No of donations				
First time	39 (4·16)	899	22 (2·35)	916
Repeat	31 (1·47)	2084	44 (2·08)	2071
	p<0·001		p=0·642	
Type of donor*				
Replacement	25 (3·82)	630	14 (2·14)	641
Voluntary	45 (1·88)	2353	52 (2·17)	2346
	p=0·003		p=0·961	
VDRL reactive (at least weakly reactive)				
Yes	3 (7·89)	35	2 (5·26)	36
No	67 (2·22)	2948	64 (2·12)	2951
	p=0·020		p=0·186	
HBsAg positive				
Yes	19 (6·93)	255	12 (4·38)	262
No	51 (1·84)	2728	54 (1·94)	2725
	p<0·001		p=0·008	

* See text for definition; VDRL = Venereal Disease Research Laboratory

graphics and several potential risk factors, including visits to prostitutes, homosexual practice, premarital/extramarital sex, and STD. The donors were also asked to make an overall assessment of whether their own blood was safe enough for transfusion. Donors who were rejected because of a history of previous blood transfusion or injecting drug use were offered free blood testing only to be included in this study. The questionnaire used in this study was specifically developed and pretested in 10 HBsAg positive blood donors. The protocol of this study was approved by the ethical committee of the Ministry of Public Health of Thailand.

Routine blood donor screening included body weight measurement, haemoglobin determination, blood pressure recording, and brief medical history interview. Potential donors with a history of malaria, previous transfusion, or injecting drug use were deferred. Blood was drawn and routinely tested for anti-HIV antibody, serology for syphilis (Venereal Disease Research Laboratory (VDRL)) and hepatitis B surface antigen (HBsAg). Test kits used for determination of anti-HIV antibody were Enzygnost anti-HIV1/HIV2 (Behring, Germany) or Genelavia Mixt (Sanofi Diagnostics Pasteur, France). If blood was shown to be HIV reactive in one test, it was retested with the other. Only repeatedly (twice) reactive results were considered anti-HIV positive. Blood units that were positive on either test were discarded. When the serum was reactive to only one of the two testings, immunoblotting was done for confirmation. VDRL (VDRL Carbon Antigen, Cambridge, Massachusetts) tests were done for *Treponema pallidum* infection. Serum shown to be at least weakly reactive was considered VDRL reactive and discarded. Test kits for HBsAg were Hepanostika HBsAg Uni-Form (Organon Teknika, The Netherlands) and Monilisa Ag HBs (Sanofi Diagnostics Pasteur, France). These two kits were used interchangeably. One positive result with either kit was considered HBsAg-positive and constituted the basis for discarding the blood. Routine testing was not performed for anti-HCV antibody.

Data were entered twice into database files and validation was done by using *EpiInfo* 5·01b (Centers of Disease Control and Prevention, Atlanta, Georgia, USA). Cross tabulation between several risk factors and anti-HIV and anti-HCV positivity was performed. Odds ratios (OR) and their associated 95% confidence intervals (95% CI) were calculated by *EpiInfo* 5·01b. Exact CIs were used when indicated.

Results

There were 3053 donations between January and March 1994. The prevalence rates of anti-HIV, anti-HCV, VDRL, and HBsAg positivity were 2·29% (70 of 3053), 2·16% (66 of 3053), 1·24% (38 of 3053) and 8·97% (274 of 3053), respectively. About half of the donors were under 35 years of age and three quarters were men. Approximately, one third were first time donors. One fifth of the donations were done to replace blood used by the donors' friends or relatives (designated as replacement donors) and the rest were from volunteer donors. As shown in table 1, young age group, male gender, first time donors, and replacement donorship were associated significantly with anti-HIV positivity, but not anti-HCV positivity. VDRL reactivity and HBsAg positivity were also associated with increased risk of anti-HIV and anti-HCV positivity, although the evidence was weaker in cases of HCV.

Of the 3053 donors, 1756 (57·5%) donated on site during office hours and were therefore invited to join the study. None of the donors refused to participate in this study. The demographics of those who were interviewed and those who were not were similar. The prevalence rates of anti-HIV (2·79%), anti-HCV (2·22%), VDRL (1·42%), and HBsAg (9·97%) positivity among this group were comparable to the whole. Table 2 compares risk factors for anti-HIV and anti-HCV positivity among this group. The associations between anti-HIV and anti-HCV antibody assays and age, sex, number of donations, type of donorship, and VDRL and HBsAg positivity were also similar to those shown in table 1 (data not shown).

Five donors had a history of injecting drug use and, therefore, were not allowed to donate. All of these donors, however, were interviewed and blood tested. None of the donors in this study had a history of blood transfusion or homosexual practice. Military donors were more likely to be anti-HIV positive than those from other occupations but this was not the case for anti-HCV positivity. Sexual risk factors were found to be associated, mostly strongly, with anti-HIV positivity – that is, premarital/extramarital sex, prostitute visit, histories of diagnosed syphilis or positive syphilis serology, genital ulcer, genital discharge, and enlarged inguinal nodes. However, again, this was not true for the associations between these risk factors and anti-HCV positivity. In contrast, anti-HCV positivity was found to be associated

Table 2 Risk factors for anti-HIV and anti-HCV positivity among blood donors

Variables	Anti-HIV			Anti-HCV		
	+Ve	−Ve	OR (95% CI)	+Ve	−Ve	OR (95% CI)
Marital status						
Single	29	363	5·4 (2·9, 10·0)	11	381	1·4 (0·6, 2·9)
Others	20	1344	1	28	1336	1
Occupation						
Military	10	52	8·2 (3·6, 18·1)	1	61	0·7 (0·0, 4·4)
Others	39	1655	1	38	1656	1
Education						
Up to primary school	38	1220	1·4 (0·7, 2·9)	28	1230	1·1 (0·5, 2·2)
Beyond primary school	11	487	1	11	487	1
Certainty that his/her own blood is safe						
Yes	42	1662	1	39	1665	1
No	7	45	6·2 (2·2, 14·8)	0	52	0·0 (0·0, 3·3)
History of hepatitis or jaundice						
Yes	0	38	0·0 (0·0, 3·6)	1	37	1·2 (0·0, 7·5)
No	49	1669	1	38	1680	1
History of being tattooed in past 3 y						
Yes	1	19	1·8 (0·0, 12·1)	2	18	5·1 (0·6, 22·6)
No	48	1688	1	37	1699	1
History premarital/extramatrial sex in past 3 mth						
Yes	11	58	8·2 (3·8, 17·7)	2	67	1·3 (0·2, 5·4)
No	38	1649	1	37	1650	1
History of unprotected sex with prostitutes in the past 3 mth (males only, n = 1308)						
Yes	4	17	6·8 (1·6, 22·0)	0	21	0·0 (0·0, 7·7)
No	43	1244	1	33	1254	1
History of injecting drug use						
Yes	0	5	0·0 (0·0, 38·8)	1	4	11·3 (0·2, 116·9)
No	49	1702	1	38	1713	1
History of diagnosed syphilis or positive syphilis serology in the past 1 y						
Yes	4	17	8·8 (2·1, 28·5)	1	20	2·2 (0·1, 14·7)
No	45	1690	1	38	1697	1
History of genital ulcer in the past 1 y						
Yes	4	9	16·8 (3·6, 62·5)	0	13	0·0 (0·0, 14·9)
No	45	1698	1	39	1704	1
History of genital discharge in the past 1 y						
Yes	2	8	9·0 (0·9, 46·8)	0	10	0·0 (0·0, 20·3)
No	47	1699	1	39	1707	1
History of painful urination in the past 1 y						
Yes	1	27	1·3 (0·0, 8·2)	0	28	0·0 (0·0, 6·4)
No	48	1680	1	39	1689	1
History of enlarged inguinal node in the past 1 y						
Yes	2	2	36·3 (2·6, 505·2)	0	4	0·0 (0·0, 68·2)
No	47	1705	1	39	1713	1

OR = odds ration, CI = confidence interval

with history of being tattooed in the past three years and history of injecting drug use, although the numbers of positive responses were small.

Discussion

The prevalence of anti-HCV antibody was comparable to the previous reports from Thailand.[1-2] This rate was similar to the rates reported from Brazil,[10-11] Kuwait,[12] and Saudi Arabia.[13] It is much higher, however, than the rates among blood donors in industrialised countries, for example, United States,[14-15] Japan,[16-17] Germany,[18] France,[19-20] Australia,[21] and much lower than among Egyptian blood donors.[13 22]

In this study, we limited the recall period for main risk behaviours to a relatively short one – the past three months – in order to avoid any effect of memory failure. This may explain in part the low frequency of reporting the risk behaviours, for example, 69 of 1756 for premarital/extramarital sex and 21 of 1756 for contact with prostitutes.

The findings on sexual risk factors for HIV infection described in this study were consistent with previous reports from northern Thailand.[23-24] Injecting drug use and being tattooed were not as important for HIV transmission in this population as they were for HCV. The importance of the parenteral transmission for HCV has been reported in other studies.[6 22 25-26] The fact that sexual risk factors did not make a significant contribution to HCV transmission in this HIV epidemic area suggests that sexual transmission plays a minor role in this part of Thailand, relative to parenteral transmission. This finding supported other studies which showed that sexual transmission of HCV occurred infrequently.[27-28]

In this study, we did not examine whether the low efficiency of sexual transmission of HCV was increased by the coexistence of HIV infection, as suggested in some studies,[29-30] because of the small number of the donors with both viruses. In addition, we found no reported risk factors in a significant proportion of HCV positive donors who were interviewed in this study. This was probably because the donors tended to under report their risk behaviours at the time of donation because they did not know that they were anti-HCV positive. The reporting frequency would probably increase if donors were interviewed after they had learned the test results, but this could be subject to recall bias. Therefore, to avoid bias, it was appropriate that donors should not know their infection status at the time of interview.

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1 Petchclai B, Srivatanakul P, Puntanee K, Hiranras S, Chiewsilp P, Kunakorn M, Liemsuwan C. Antibodies to hepatitis C virus among patients with hepatocellular carcinoma and blood donors in Thailand. *J Med Assoc Thail* 1992;**75**(suppl 1):68–71.
2 Boonmar S, Pojanagaroon B, Watanabe Y, Tanaka Y, Saito I, Miyamura T. Prevalence of hepatitis C virus antibody among healthy blood donors and non-A, non-B hepatitis patients in Thailand. *Jpn J Med Sci Biol* 1990;**43**:29–36.
3 Esteban JI, Esteban R, Viladomiu K, *et al.* Hepatitis C virus antibodies among risk groups in Spain. *Lancet* 1989;ii: 294–7.
4 McKenna JG, Evans G, Lyttle PH, Couper A. Hepatitis C virus seroprevalence in patients attending a sexual health centre. *New Zealand Med J* 1994;**107**(970):8–10.
5 Thomas DL, Cannon RO, Shapiro CN, Hook EW 3rd, Alter MJ, Quinn TC. Hepatitis C, hepatitis B, and human immunodeficiency virus infections among non-intravenous drug-using patients attending clinics for sexually transmitted diseases. *J Infect Dis* 1994;**169**(5):990–5.
6 Neal KR, Jones DA, Killey D, James V. Risk factors for hepatitis C virus infection. A case-control study of blood donors in the Trent Region (UK). *Epidemiol Infect* 1994; **112**(3):595–601.
7 Takeuchi K, Kubo Y, Boonmar S, *et al.* The putative nucleocapsid and envelope protein genes of hepatitis C virus determined by comparison of the nucleotide sequences of two isolates derived from an experimentally infected chimpanzee and healthy human carriers. *J Gen Virol* 1990;**71**(12):3027–33.
8 Takeuchi K, Boonmar S, Kubo Y, *et al.* Hepatitis C virus cDNA clones isolated from a healthy carrier donor implicated in post-transfusion, non-A, non-B hepatitis. *Gene* 1990;**91**(2):287–91.
9 Katayama T, Mazda T, Kikuchi S, *et al.* Improved serodiagnosis of non-A, non-B hepatitis by an assay detecting antibody to hepatitis C virus core antigen. *Hepatology* 1992;**15**:391–4.
10 Vanderborght BO, Reis AM, Rouzere CD, *et al.* Prevalence of anti-hepatitis C virus in the blood donor population of Rio de Janeiro. *Vox Sang* 1993;**65**(2):122–5.
11 Patino-Sarcinelli F, Hyman J, Camacho LA, Linhares DB, Azevedo JG. Prevalence and risk factors for hepatitis C antibodies in volunteer blood donors in Brazil. *Transfusion* 1994;**34**(2):138–41.
12 Al-Nakib B, Koshy A, Kaloui M, Al-Ramahi S, Al-Mufti S, Radhakrishnan S, Al-Nakib W. Hepatitis C virus antibody in Kuwait. (letter). *Vox Sang* 1992;**63**:75–6.

13 Abdelaal M, Rowbottom D, Zawawi T, Scott T, Gilpin C. Epidemiology of hepatitis C virus: a study of male blood donors in Saudi Arabia. *Transfusion* 1994;**34**(2):135–7.
14 Stevens CE, Taylor PE, Pindyck J, Choo QL, Bradley DW, Kuo G, Houghton M. Epidemiology of hepatitis C virus. A preliminary study in volunteer blood donors. *JAMA* 1990;**263**(1):49–53.
15 Richards C, Holland P, Kuramoto K, Douville C, Randell R. Prevalence of antibody to hepatitis C virus in a blood donor population. *Transfusion* 1991;**31**(2):109–13.
16 Miyamura T, Saito I, Katayama T, *et al.* Detection of antibody against antigen expressed by molecularly cloned hepatitis C virus cDNA: Application to diagnosis and blood screening for posttransfusion hepatitis. *Proc Natl Acad Sci USA* 1989;**87**:983–7.
17 Shimoyama R, Sekiguchi S, Suga M, Sakamoto S, Yachi A. The epidemiology and infection route of asymptomatic HCV carriers detected through blood donations. *Gastroenterol Jpn* 1993;**28**(suppl 5):1–5.
18 Kühnl P, Seidl S, Stangel W, Beyer J, Sibrowshi W, Flik J. Antibody to hepatitis C virus in German blood donors. (letter). *Lancet* 1989;ii:324.
19 Janot C, Courouce AM, Maniez M. Antibodies to hepatitis C virus in French blood donors. *Lancet* 1989 Sept 30;ii: 796–7.
20 Ranger S, Martin P, Roussanne MC, Denis F. Prevalence of hepatitis C virus antibodies in the general population and in selected groups of patients in Limoges, France. *Gut* 1993;**34**(suppl):S50–S51.
21 Archer GT, Buring ML, Clark B, *et al.* Prevalence of hepatitis C virus antibodies in Sydney blood donors. *Med J Aust* 1992;**157**(4):225–7.
22 Darwish MA, Raouf TA, Rushdy P, Constantine NT, Rao MR, Edelman R. Risk factors associated with a high seroprevalence of hepatitis C virus infection in Egyptian blood donors. *Am J Trop Med Hyg* 1993;**49**(4):440–7.
23 Nelson KE, Celentano D, Suprasert S, *et al.* Risk factors for human immunodeficiency virus infection among young men in Thailand. *JAMA* 1993;**270**:955–60.
24 Nopkesorn T, Mastro TD, Sangkharomya S, *et al.* HIV-1 infection in young men in northern Thailand. *AIDS* 1993; 7:1233–9.
25 van der Poel C, Cuypers H, Reesink H, *et al.* Risk factors in hepatitis C virus-infected blood donors. *Transfusion* 1991;**31**(8):777–9.
26 Serfaty L, Giral P, Elghouzzi MH, Jullien AM, Poupon R. Risk factors for hepatitis C virus infections in hepatitis C virus antibody ELISA-positive blood donors according to RIBA-2 status: a case-control survey. *Hepatology* 1993; **17**(2):183–7.
27 Osmond DH, Charlebois E, Sheppard HW, Page K, Winkelstein W, Moss AR, Reingold A. Comparison of risk factors for hepatitis C and hepatitis B virus infection in homosexual men. *J Infect Dis* 1993;**167**(1):66–71.
28 Weinstock HS, Bolan G, Reingold AL, Polish LB. Hepatitis C virus infection among patients attending a clinic for sexually transmitted diseases. *JAMA* 1993;**269**(3):392–4.
29 Eyster ME, Alter HJ, Aledort LM, Quan S, Hatzakis A, Goedert JJ. Heterosexual co-transmission of hepatitis C virus (HCV) and human immunodeficiency virus (HIV). *Ann Intern Med* 1991;**115**(10):764–8.
30 Lissen E, Alter HJ, Abad MA, *et al.* Hepatitis C virus infection among sexually promiscuous groups and the heterosexual partners of hepatitis C virus infected index cases. *Eur J Clin Microbiol Infect Dis* 1993;**12**(11):827–31.