Association of HCV and *Treponema pallidum* Infection in HIV Infected Northeastern Thai Male Blood Donors

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Abstract

The study was performed to determine the association of seroprevalence of hepatitis C virus (HCV) and *Treponema pallidum* (*T. pallidum*) infection among HIV infected first time male blood donors (HIV group) in comparison with the HIV seronegative blood donors (control group) in the Northeast of Thailand (NET). Serum samples were collected from 10,321 first blood donation voluntary male donors. All samples were screened for anti-HIV and anti-HCV by particle agglutination test, and syphilis antibody by RPR. The anti-HIV positive sera were repeated by EIA and confirmed by western blot. The reactive anti-HCV samples were confirmed by EIA whereas reactive syphilis antibody samples were confirmed by TPPA. Fisher's exact test was used for statistical analysis. The prevalence of anti-HIV in first time male donors was 0.70 per cent (72/10,321). The age of HIV group and 10,018 male control group ranged from 17-50 years old. The prevalence of HIV among 21-40 years old age group was significantly higher than the 17-20 years old ($p=0.00003$). The 17-20 years old HIV group showed significantly higher seroprevalence of TPPA ($p=0.003$). The 21-30 years old HIV group gave significantly higher seroprevalence of anti-HCV ($p=0.0008$) and TPPA ($p=0.045$), but the seroprevalence of anti-HCV and TPPA among the 31-50 year old group were nonsignificantly different ($p > 0.05$). The concurrence of anti-HCV and TPPA in HIV groups was not found.

This result indicated that HIV infection among NET voluntary male blood donors was significantly associated with *T. pallidum* infection in young adults and the HCV infection in mature adults.

The hepatitis C virus (HCV) was discovered in 1989 by Choo et al[1]. It is the main cause of non-A, non-B hepatitis (NANBH)[2]. HCV frequently caused chronic hepatitis[3]. The sequels to chronic hepatitis C are potentially substantial. Up to 20 per cent of patients with chronic hepatitis C develop cirrhosis within 5 years[4]. Hepatocellular carcinoma may develop in cirrhotic

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livers; there may be no prominent signs until the cancer signals severe liver disease[5]. Although the route of HCV transmission *via* blood is like HIV, in most cases the route is not identified[6]. The prevalence of anti -HCV suggested a rather high prevalence rate among blood donors varying from 0.5 per cent to 1.5 per cent in Southern Europe, the United States, Japan and Northeastern Thailand[6,7], to more than 10 per cent in Egypt[6]. Syphilis is one of the major sexually transmitted diseases (STD) which is a systemic disease caused by the spirochete *Treponema pallidum* (*T. pallidum*). Sexual transmission of *T. pallidum* occurs when mucocutaneous syphilitic lesions are presented. Syphilis patients may seek treatment for symptoms of primary, secondary or tertiary infection. Infections may also be detected during the latent stage by two types of serological testing : nontreponemal antibody (VDRL, RPR) and treponemal antibody (FTA-ABS, TPHA)[8,9]. The use of one type of test alone is not sufficient for diagnosis. Nontreponemal test antibody titer is usually more correlated with disease activity than treponemal antibody testing. Both treponemal and nontreponemal serological tests for syphilis are accurate for patients with syphilis and HIV coinfection[8,9]. Epidemiological studies have suggested an association between HIV infection and past or present infection with other STD[10]. The HIV epidemic in Thailand has been attributed largely to heterosexual transmission[11,12]. It is also possible that STDs infection may influence the probability that a person will acquire HIV.

This study was performed to determine the association of seroprevalences of HCV and *T. pallidum* infections among HIV infected male blood donors for comparison with the HIV seronegative blood donors in the Northeast of Thailand (NET).

MATERIAL AND METHOD

Study design:

A cross sectional method was carried out from January 1995 to February 1997 at the Blood Transfusion Centre, Faculty of Medicine, Khon Kaen University. A total of 10,321 serum samples were obtained from first time voluntary male blood donors. The association study for HCV and *T. pallidum* infections among HIV seropositive (HIV group) were analysed in comparison to the results obtained from HIV seronegative (control group) with the same range of age. There were 72 HIV seropositive with the age ranging from 17-50 years old and 10,018 cases of control group in the same age range.

Serological assays:

Anti-HIV was tested by particle agglutination (PA, serodia-HIV, Fujirebio, Japan) and confirmed by western blot (Diagnostic Biotechnology, Singapore). Anti-HCV was tested by particle agglutination (PA, serodia-HCV, Fujirebio, Japan) and reactive samples were retested by EIA (Detect-HCV version 2.5, Biochem Immunosystems, Canada). The samples which were positive by PA and EIA were considered as positive anti-HCV. Syphilis antibody was screened by nontreponemal test (RPR - Porton, Cambridge, U.K.). The reactive samples were confirmed by *T. pallidum* particle agglutination test (serodia-TPPA, Fujirebio, Japan) which has the same principle as TPHA technique except using gelatin particle instead of red blood cell.

Statistical analysis:

The seroprevalence of anti-HCV and TPPA antibodies among HIV seropositive (HIV group) and HIV seronegative (control group) voluntary first time male blood donors in various ages was analysed. The statistical analysis was done by Fisher's exact test with 95 per cent confidence interval (95% CI) from statistical software (Epi Info version 5.0)[13].

Table 1. Anti-HIV positive among first time voluntary male blood donors in Northeastern Thailand during January 1995 to February 1997.

Age range (yrs)	No. tested	No. positive (%)	p -value *versus* 17-20 years old age group
17-20	3,719	4 (0.11)	-
21-30	3,635	52 (1.43)	< 0.00001
31-40	1,752	15 (0.86)	0.00003
41-50	984	1 (0.10)	NS
51-60	231	0 (0)	NT
Total	10,321	72 (0.70)	

NS = nonsignificant difference ($p > 0.05$)
NT = not tested

Table 2. The seroprevalence of anti-HCV and TPPA among first time male blood donors in the HIV seropositive (HIV group) compared to the HIV seronegative (control group) in various age groups.

Age range (yr)	Group	No.	Number positive (%)				
			HCV + TPPA -	HCV - TPPA +	HCV + TPPA +	total anti-HCV	total TPPA
17-20	HIV	4	0(0)	1(25.00)	0(0)	0(0)	1(25.00)
	Control	3715	67(1.80)	2(0.05)	0(0)	67(1.80)	2(0.05)
						NS	p=0.003
21-30	HIV	52	10(19.23)	2(3.85)	0(0)	10(19.23)	2(3.85)
	Control	3583	206(5.75)	20(0.56)	2(0.06)	208(5.81)	22(0.61)
						p=0.0008	p=0.045
31-40	HIV	15	3(20)	1(6.67)	0(0)	3(20)	1(6.67)
	Control	1737	145(8.35)	23(1.32)	5(0.29)	150(8.64)	28(1.61)
						NS	NS
41-50	HIV	1	0(0)	0(0)	0(0)	0(0)	0(0)
	Control	983	27(2.75)	26(2.64)	2(0.20)	29(2.95)	28(2.85)
						NS	NS

NS = nonsignificant difference (p > 0.05)

RESULTS

The prevalence of anti-HIV among the first time NET male blood donors was 0.70 per cent (72/10,320). All of the 72 cases of HIV group were less than 50 years old. There were 1.43 per cent (52/3,635) in the 21-30 year old group and 0.86 per cent (15/1,752) in the 31-40 year old group. There were 10,018 control group in 17-50 year old range. All of the 51-60 year old group were anti-HIV negative (Table 1). The seroprevalence of anti-HIV was significantly higher in the 21-40 year old group than in the 17-20 year group (p<0.00003).

Table 2 showed that the seroprevalences of anti-HCV and TPPA among the HIV group were 18.06 per cent (13/72) and 5.56 per cent (4/72), respectively. The seroprevalences of anti-HCV and TPPA among control group were 4.53 per cent (454/10,018) and 0.80% (80/10,018), respectively. The concurrence of anti-HCV and TPPA was 0.09 per cent (9/10,018) in the control group, but it was not found in the HIV group.

In the 17-20 year old group, the seroprevalences of anti-HCV and TPPA among the HIV group were 0 per cent (0/4) and 25.0 per cent (1/4), respectively. The seroprevalences of anti-HCV and TPPA among the control group were 1.80 per cent (67/3,715) and 0.05% (2/3,715), respectively. The concurrence of anti-HCV and TPPA was not found in both the HIV group and control group. There was significantly higher seroprevalence of TPPA (p=0.003).

In the 21-30 year old group, the seroprevalences of anti-HCV and TPPA among the HIV group were 19.23 per cent (10/52) and 3.85 per cent (2/52), respectively. The seroprevalences of anti-HCV and TPPA among control group were 5.81 per cent (208/3,583) and 0.61 per cent (22/3,583), respectively. The concurrence of anti-HCV and TPPA was 0.06 per cent (2/3,583) in the control group. There was significantly higher seroprevalence of anti-HCV (p=0.0008) and TPPA (p=0.045).

In the 31-50 year old group, the seroprevalence of anti-HIV and TPPA were not significantly different to the control group (p>0.05).

DISCUSSION

The prevalence of anti-HIV among voluntary first time NET male blood donors from 1995 to early 1997 was 0.70 per cent. The seroprevalence of anti-HIV was significantly higher in the 21-40 year old group than the 17-20 year old (p=<0.00001, p=0.00003). According to the study for

the association of HIV seroconversion, *T. pallidum* and HCV, it was found that HIV infection among male blood donors was significantly associated with *T. pallidum* and HCV infections.

Many data demonstrating a significant correlation between HIV and syphilis has been seen in intravenous drug users (IVDU)[14], STD patients[15], and homosexual men[16]. Petersen et al showed that there was about 14 times greater chance of serological reactive for syphilis blood donors than the nonreactive blood donor[17]. Our data support other reports that a reactive serology for syphilis was the potential risk factor and most consistently correlated with HIV infection in blood donors[18,19]. Otten et al showed that primary or secondary syphilis was highly correlated with subsequent HIV infection in a STD clinic[20]. It is possible that syphilitic lesions may facilitate the transmission of HIV[16]. A correlation between seropositivity for syphilis and hepatitis B is equally well established[19]. Mc Quillan et al showed that the seroprevalence of hepatitis B virus found in an individual with a positive FTA was seven times higher than in an individual with a negative FTA[21]. This study verifies that syphilis serology is related to the prevalence of active sexually transmitted diseases in the young adult NET blood donors. Syphilis will continue to have some value as a surrogate test for HIV, hepatitis B and hepatitis C, but this is likely to be effective only in countries or populations with a significant risk of heterosexually acquired HIV or other STD. Detection of the HIV window period donor is believed to represent the most significant threat to the safety of the blood supply. The value of syphilis serology is as a surrogate test for HIV and hepatitis B seroconversion. It was thought that similar results would apply to blood donors. It is also possible that the serology to syphilis (STS) may have greater value in the undiscovered transfusion-associated and sexually transmitted pathogen appearing in the blood supply.

Our data demonstrated statistically significant association of anti-HIV with HCV infection in mature adults ($p = 0.0008$). HCV is transmitted mainly *via* blood, while transmission *via* other body fluids is uncommon. The route of transmission in most cases is not identified[6]. A number of studies have addressed the question of sexual transmission of HCV, the results are somewhat conflicting. Hyams et al indicated that having a large number of sexual partners is a risk factor of sexual transmission of HCV[22], while the others found that the risk of sexual transmission of HCV is absent or very low[23,24].

Infection of HIV and *T. pallidum* in the majority of people was by sexual contact transmission[12]. Prevention and control of STD are based on four major concepts. Firstly, education to reduce the risk of transmission. Secondly, detection of asymptomatically infected persons. Thirdly, effective diagnosis and treatment of infected persons. Finally, evaluation, treatment, and counselling of infected sex partners[8,25]. Although this document deals largely with secondary prevention, the primary prevention of STD is based on changing sexual behavior. Condom users appear to be associated with low risk to STD[25,26]. However, condom users was low in young Thai men[27].

In conclusion, the results of this study not only provide correlation between HIV and syphilis in young adults but also provide correlation between HIV and HCV in mature adult blood donors in NET. Further studies are needed to determine the cofactor of HCV and *T. pallidum* coinfection in this group.

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ความสัมพันธ์ของการติดเชื้อไวรัสตับอักเสบซีและซิฟิลิสในผู้บริจาคโลหิตชายไทยอีสานซึ่งติดเชื้อไวรัสเอชไอวี

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เพื่อศึกษาความสัมพันธ์ของการติดเชื้อไวรัสตับอักเสบซี ซิฟิลิส และเอชไอวีจากกลุ่มผู้บริจาคโลหิตครั้งแรกชายไทยอีสาน โดยตรวจกรอง anti-HIV, anti-HCV ด้วยวิธี Particle agglutination (PA) และตรวจกรอง syphilis antibody ด้วยวิธี RPR จากนั้นตรวจยืนยันผลบวก anit-HIV ด้วยวิธี Western blot, anti-HCV ด้วยวิธี EIA และ syphilis antibody ด้วยเทคนิค TPPA ผลการศึกษาพบผู้บริจาคโลหิตเพศชายติดเชื้อเอชไอวีจำนวนทั้งสิ้น 72 ราย คิดเป็นร้อยละ 0.70 (72/10,321) ทั้งหมดอยู่ในช่วงอายุ 17-50 ปี โดยมีอัตราพบในช่วงอายุ 21-40 ปีมากกว่าช่วงอายุ 17-20 ปีอย่างมีนัยสำคัญ (p=0.00003) เมื่อศึกษาความสัมพันธ์ของการติดเชื้อ HCV, syphilis และ HIV ในกลุ่มตัวอย่างช่วงอายุ 17-50 ปีจำนวน 10,090 ราย แยกเป็นกลุ่มที่ตรวจพบการติดเชื้อเอชไอวี (กลุ่ม HIV) จำนวน 72 ราย และกลุ่มที่ไม่พบการติดเชื้อเอชไอวี (กลุ่มควบคุม) จำนวน 10,018 ราย พบว่ากลุ่ม HIV ช่วงอายุ 17-20 ปี จะมีอัตราการพบผลบวก TPPA (p=0.003) และกลุ่ม HIV ช่วงอายุ 21-30 ปี จะมีอัตราการพบ ผลบวก anti-HCV (p=0.0008), TPPA (p=0.045) สูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ แต่กลุ่ม HIV ช่วงอายุ 31-50 ปี มีอัตราพบผลบวก anti-HCV และ TPPA ไม่แตกต่างกับกลุ่มควบคุมอย่างมีนัยสำคัญ (p>0.05) ในกลุ่ม HIV จะไม่พบ anit-HCV ร่วมกับ TPPA ในผู้บริจาครายเดียวกันเลย

ผลการศึกษาสรุปได้ว่าการติดเชื้อเอชไอวีในผู้บริจาคโลหิตชายชาวไทยอีสานจะมีความสัมพันธ์ต่อการติดเชื้อ *T. pallidum* ในช่วงวัยรุ่นและมีความสัมพันธ์ต่อการติดเชื้อไวรัสตับอักเสบซีในช่วงย่างสู่วัยผู้ใหญ่

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