Factors Associated with Hepatitis C Infection among Patients with Skin Diseases

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Objective: *The present study attempted to assess factors associated with positive anti-HCV among patients with skin diseases.*
Material and Method: *A retrospective analysis of 3,496 subjects' history profiles from the HCV antibody surveillance projects performed from 2000 to 2007. Only 150 subject profiles with skin diseases were included in the analysis of factors associated with positive anti-HCV. Patient profiles including socio-demographic parameters, the main risk behavior or risk exposure, types of skin diseases, anti-HIV status, and results of anti-HCV were analyzed using Chi-square test or Fisher's exact test.*
Results: *Results revealed that only 10 from 150 studied patients (6.7%) were positive for anti-HCV antibody. Patient profiles including socio-demographic parameters, the main risk behavior or risk exposure, types of skin diseases, and anti-HIV status among patients with or without anti-HCV were compared and analyzed to assess factors associated with positive anti-HCV. It was found that patient's income, types of skin disease, and anti-HIV status were significantly associated with positive anti-HCV among this group, p = 0.0240, p = 0.0053 and p = 0.0462, respectively.*
Conclusion: *This analysis found three studied factors including patient's income, types of skin disease, and anti-HIV status to be significantly associated with HCV infection in patients with skin diseases. However, a large-scale work should be done to confirm the present study.*

Keywords: *Anti-HCV, Anti-HIV, Skin diseases, Retrospective analysis*

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Hepatitis C virus (HCV) infection is a global public health problem. Approximately 2.2-3% of the world population or estimated 170 million people are already infected with HCV[1,2]. According to previous studies in Thailand, the prevalence has variably been estimated to be between 1.5% to 4.5% among the blood donors and general population depending on regions of the study[3-7]. The infection progresses into chronic liver disease and leads to liver cirrhosis and hepatocellular carcinoma (HCC), one of the most common cancers in Asian countries and sub-Saharan Africa[8-11]. HCV infection was the highest risk factor for HCC in Japan which markers of HCV infection were found in 80% to 90% of patients with HCC[11]. Additionally, HCV infection may contribute to faster progression and higher incidence rates of liver cirrhosis and HCC among HIV-coinfected patients than those without HIV-coinfection[9,11-13].

The transmission route of HCV is via the parenteral route, especially injecting drug use, unhygienic tattooing or ear piercing and receiving unscreened blood, blood products and donated organs with a minority contracting the virus through sexual contact[2,4,5,7]. In order to prevent the HCV transmission and to reduce the burden of liver diseases and HCC, the screening of blood, blood products and donated organs, using sterile dental and medical instruments, and avoiding some risk behaviors, such as injecting drug use, tattooing, and high risk sexual practices should be emphasized[2,13-15].

Both acute and chronic HCV infection can manifest on the skin dermatologists reported. Several studies in recent years have shown that cutaneous manifestations, such as urticaria, pruritus, lichen planus, and cutaneous vasculitis occur in approximately 20-40% of the patients with chronic HCV infection[16-22]. According to limited data about HCV infection and skin disorders in Thai patients and population, this retrospective analysis was carried out to assess factors

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associated with positive anti-HCV in patients with skin diseases.

Material and Method

Study design and study subjects

A retrospective analysis of 3,496 subjects' history profiles from the HCV antibody surveillance projects performed from 2000 to 2007 in Microbiology Department, Faculty of Public Health, Mahidol University was carried out. The researcher set the inclusion criteria as subject profiles with skin diseases such as pruritic eruption, urticaria, eczema, psoriasis, and skin infections with herpes zoster, herpes simplex, bacteria, and fungi, male and female, and every age group. Only 150 subject history profiles met the criteria and were included in the present study analysis. From subject history profiles, all of them were patients seeking medical treatment at an outpatient department of some governmental hospitals in Bangkok, and the hospital laboratory sent the patient sera and their information to the department following the HCV antibody surveillance projects. The subject history profiles including socio-demographic parameters, the main risk behavior or risk exposure, types of skin diseases, anti-HIV status, and laboratory results of anti-HCV antibody were reviewed and analyzed.

Methods of anti-HCV testing and data analysis

The presence of anti-HCV antibody was detected by the third generation method of ABBOTT HCV Enzyme Immunoassay (EIA) with more than 97% sensitivity and specificity. Cut-off value for anti-HCV reactivity followed the criteria of ABBOTT HCV EIA 3.0 and was equal to or greater than 0.387. Serum samples yielding a positive anti-HCV were tested twice.

Ethical approval

The Ethics Committee of Faculty of Public Health, Mahidol University reviewed the study protocol and classified this study into an exempted project.

Data analysis

Data were analyzed by descriptive statistics, such as number and percentage. The statistical significance was expressed as p-value by the Chi-square test or Fisher's exact test. The critical level of $p<0.05$ was considered statistically significant.

Results

Study patient profiles and positive anti-HCV

One hundred and fifty patient history profiles were enrolled, 71.3% aged 21-40 years. Male to female ratio was 2.75:1 (73.3% vs. 26.7%). Approximately 62% had secondary education level and lower. The occupation was mostly workers and officers (77.3%), and 46.7% had income per month equal to 10,000 baht or less. About 48% had a main risk behavior because of sexual contact without using condom, and 53.3% had chronic skin diseases. Details are shown in Table 1. Out of 150 patient history profiles, 6.7% (10 individuals) were positive for the anti-HCV antibody. Nine out of ten positive anti-HCV subjects were male, and 8 were positive anti-HIV. Five patients had skin infections (3 cases with herpes infection and 2 cases with bacterial

Table 1. Percentage of positive anti-HCV subjects with skin diseases

Variables	No. (%)
Age (years)	
<20	14 (9.3)
20-40	107 (71.3)
>40	29 (19.4)
Gender	
Male	110 (73.3)
Female	40 (26.7)
Marital status	
Single	48 (32.0)
Married	77 (51.3)
Widowed, divorced, separated	25 (16.7)
Education	
Secondary level and lower	93 (62.0)
Technical level	40 (26.7)
University level	17 (11.3)
Income/month (Baht)	
≤10,000	19 (12.7)
10,001-20,000	119 (79.3)
>20,000	12 (8.0)
Occupation	
Workers	71 (47.3)
Officers	48 (32.0)
Others (such as student, housewife, ect.)	31 (20.7)
Main risk behaviors	
Injecting drug use	6 (4.0)
Sexual contact without condom	72 (48.0)
History of jaundice	8 (5.3)
No main risk behavior identified	64 (42.7)
Skin disorders	
Chronic skin disease (such as psoriasis and pruritic eruption)	80 (53.3)
Skin infection	26 (17.3)
Eczema	25 (16.7)
Others (such as SLE with vasculitis, exfoliative dermatitis, exanthema, ect.)	19 (12.7)

infection), the rest were psoriasis, eczema, and pruritic eruption. Details are shown in Table 2.

Factors associated with positive anti-HCV among patients with skin diseases

To study some factors associated with positive anti-HCV among this studied group, interested variables of subject history profiles of patients with HCV antibody and those without HCV antibody were compared and analyzed. The results revealed that patient's income/month, types of skin diseases, and anti-HIV status were significantly associated with positive anti-HCV among this group, p = 0.0240, 0.0053, and 0.0462, respectively. Details are shown in Table 3.

Discussion

The present study found that 6.7% of 150 Thai patient profiles with skin diseases were positive for anti-HCV antibody which was higher than that in the blood donors and general population (1.5-4.5%)[3-7]. However, this finding was performed from a retrospective analysis of several HCV surveillance projects from 2000 to 2007 that a systematic bias probably occurred. The percentage of positive anti-HCV in the present study was lower than previous studies of skin diseases patients in other Asian countries such as 12% positive anti-HCV in Saudi Arabia skin patients[22] and 13.4% in Pakistani skin patients[23]. Garcia-Carrasco and Escarcega (2006) reported that HCV patients with extra-hepatic manifestations, such as skin disorders, could be generally seen in the late stages of the disease[19]. Urticaria and porphyria cutanea tarda were the classical skin manifestations of chronic HCV infection[19,23].

In details, the positive anti-HCV patients in the present study included subject profiles with skin infection (both viral and bacterial infections), subjects with eczema, and subjects with pruritic eruption and psoriasis. The findings differed from recent studies in other Asian countries, which have shown lichen planus, urticaria, palpable prupura and prurigo as the predominant extra-hepatic skin manifestations among chronic HCV patients[19,21,23]. The present study might be affected by HIV infection because 8 of 10 skin disease patients with positive anti-HCV were coinfected with HIV. Several studies demonstrated that most of patients with HIV/AIDS developed skin diseases, such as bacterial infection and herpes infection, eczema, and psoriasis[24-26]. A study in 651 Chinese HIV-patients who had not received highly active anti-retroviral therapy (HAART), 81.6% had skin lesions including 22.9% of

Table 2. Some characteristics of positive anti-HCV patients

Serial No.	Gender	Age (years)	Marital status	Education	Occupation	Main risk behavior	Skin diseases	Anti-HIV
1	Male	34	Married	Primary	Worker	IDU	PPE	+
2	Male	26	Married	Primary	Worker	IDU	Infection	+
3	Male	31	Single	Primary	Worker	Sexual	Eczema	+
4	Male	19	Single	Technical	Student	IDU	Infection	+
5	Male	48	Married	Secondary	Worker	Sexual	Infection	+
6	Male	32	Single	Primary	Worker	IDU	Eczema	+
7	Male	34	Single	Primary	Worker	Sexual	Psoriasis	+
8	Male	39	Single	Primary	Worker	IDU	Psoriasis	+
9	Male	43	Single	Secondary	Officer	Jaundice	Infection	-
10	Female	30	Married	Technical	Officer	No	Infection	-

IDU = injecting drug use, Sexual = sexual contact without condom, PPE = pruritic eruption

Table 3. Some factors associated with positive anti-HCV among studied patients with skin diseases

Studied variables	Positive anti-HCV individuals No. (%)	Negative anti-HCV individuals No. (%)	p-value from Chi-square or Fisher's Exact test
Age (years)			
≤40	8 (80.0)	67 (47.9)	0.1017
>40	2 (20.0)	73 (52.1)	
Gender			
Male	9 (90.0)	101 (72.1)	0.2906
Female	1 (10.0)	39 (27.9)	
Marital status			
Single	6 (60.0)	97 (69.3)	0.5055
Married	4 (40.0)	43 (30.7)	
Education			
≤ secondary level	8 (80.0)	85 (60.7)	0.3195
Higher than secondary level	2 (20.0)	55 (39.3)	
Occupation			
Workers	7 (70.0)	63 (45.0)	0.1896
Others	3 (30.0)	77 (55.0)	
Income/month (Baht)			
≤10,000	4 (40.0)	15 (10.7)	0.0240**
>10,000	6 (60.0)	125 (89.3)	
Main risk behaviors			
Yes	9 (90.0)	96 (68.6)	0.2839
No	1 (10.0)	44 (31.4)	
Types of skin disorders			
Skin infection*	5 (50.0)	16 (11.4)	0.0053**
Others	5 (50.0)	124 (88.6)	
Anti-HIV status			
Positive	8 (80.0)	62 (44.3)	0.0462**
Negative	2 (20.0)	78 (55.7)	

* Herpes zoster and herpes infection and bacterial infection
** Significance at $\alpha = 0.05$

viral infection, 26% of bacterial infection, 10.6% of dermatophytosis, 19.2% of eczema, and 0.5% of psoriasis[26]. These figures tended to be or were in concordance with our study of which most positive anti-HCV skin disorder subjects were co-infected with HIV/AIDS. Osborne et al (2003) demonstrated that HIV patients with lower CD_4^+ cell counts were prone to infectious skin diseases[24], and Huang et al (2011) revealed that infectious skin diseases were the highest common skin disorders in patients with HIV/AIDS[26].

An analysis of studied factors associated with positive anti-HCV found an association between patient's monthly income, types of skin diseases, and anti-HIV status of studied patient profiles and positiveness of anti-HCV, $p<0.05$. Low income was an indirect factor to increase the risk opportunity for HCV infection. Previous studies demonstrated that individuals with lower monthly income had significantly higher prevalence of anti-HCV than those with higher monthly income and found that the higher prevalence of anti-HCV was correlated with the low socio-economic conditions[3,27]. Additionally, it was found that types of skin diseases and status of anti-HIV were significantly associated with the anti-HCV positiveness among this group ($p = 0.0053$ and 0.0462, respectively) supported by several studies[16,18,20,26]. Skin infection with virus or bacteria showed a higher proportion of positive anti-HCV skin disease patients that probably had an effect on HIV infection[26].

Several aspects and limitations of the present study should be considered. Firstly, this study is a retrospective analysis of our subject history profiles with a small group of skin disorder patients, the effect of sample size on the statistical significance may be found. Secondly, the HCV infection in the present study was used only for anti-HCV antibody detection by the

third generation method of ABBOTT HCV Enzyme Immunoassay with high sensitivity up to 97%[28]. HCV-RNA PCR, of which the cost of testing is prohibitive particularly in a resources-limited setting, was not detected. Some HCV infected individuals were probably missed. Finally, our 10 anti-HCV positive subjects, most of them (8 subjects) were co-infected with HIV/AIDS; the pattern or occurrence of skin disorders probably differed from patients with only HCV infection due to being affected by HIV/AIDS. However, there are limited reports on the HCV patients with skin disorders in Thailand. The study on extra-hepatic manifestations, especially skin disorders in chronic hepatitis C, should be done on a large scale or with a population-based epidemiological undertaking.

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Potential conflicts of interest

None.

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ปัจจัยที่มีความสัมพันธ์กับการติดเชื้อไวรัสตับอักเสบ ซี ในผู้ป่วยโรคผิวหนัง

พิพัฒน์ ลักษมีจรัลกุล, สมใจ จันทวรลักษณ์

วัตถุประสงค์: *เพื่อวิเคราะห์ปัจจัยที่มีความสัมพันธ์กับการติดเชื้อไวรัสตับอักเสบ ซีในผู้ป่วยโรคผิวหนัง*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาย้อนหลังจากฐานข้อมูลบุคคลตามโครงการการเฝ้าระวังไวรัสตับอักเสบ ซี ที่ปฏิบัติการระหว่างปี พ.ศ. 2545 ถึง พ.ศ. 2550 จำนวนนี้มีเพียง 150 ราย ที่มีประวัติเป็นโรคผิวหนังตามเกณฑ์การคัดเข้าเพื่อวิเคราะห์ปัจจัยที่มีความสัมพันธ์กับการติดเชื้อไวรัสตับอักเสบ ซี ในการศึกษานี้ได้นำตัวแปรที่สนใจศึกษาได้แก่ ปัจจัยด้านสังคมประชากร ชนิดของโรคผิวหนัง ผลการติดเชื้อเอชไอวีและผลการตรวจการติดเชื้อไวรัสตับอักเสบ ซี มาวิเคราะห์โดยใช้ Chi-square test หรือ Fisher's exact test*

ผลการศึกษา: *พบว่าในผู้ป่วยโรคผิวหนัง 150 ราย มีการติดเชื้อไวรัสตับอักเสบ ซี 10 ราย คิดเป็นร้อยละ 6.7 เมื่อนำตัวแปรที่สนใจศึกษามาวิเคราะห์ปัจจัยที่มีความสัมพันธ์กับการติดเชื้อไวรัสตับอักเสบ ซี ในผู้ป่วยโรคผิวหนังพบว่า รายได้ผู้ป่วย ชนิดของโรคผิวหนัง สภาวะการติดเชื้อเอชไอวี มีความสัมพันธ์กับการติดเชื้อไวรัสตับอักเสบ ซี อย่างมีนัยสำคัญทางสถิติ, $p = 0.0240$, $p = 0.0053$ และ $p = 0.0462$ ตามลำดับ*

สรุป: *การศึกษาข้อมูลย้อนหลังครั้งนี้ พบ 3 ปัจจัยที่ศึกษา ได้แก่ รายได้ผู้ป่วย ชนิดของโรคผิวหนัง สภาวะการติดเชื้อเอชไอวี มีความสัมพันธ์กับการติดเชื้อไวรัสตับอักเสบ ซี อย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตามการศึกษาในกลุ่มตัวอย่างที่มีจำนวนมากกว่านี้เพื่อยืนยันผลการศึกษาครั้งนี้ ควรมีการดำเนินการต่อไป*