

Received: 2015.11.01
Accepted: 2015.11.13
Published: 2015.11.30

Effect of Patient Education Seminars on Awareness and Behavior of Individuals with Viral Liver Disease

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEG 1,2
ABC 1
DG 3
CDF 1,4
Yumiko Nagao
Yuji Kawahigashi
Michio Sata
Haruhiko Nobayashi

1 Department of Organ System Interactions and Information, Saga Medical School, Nabeshima, Saga, Japan
2 Research Center for Innovative Cancer Therapy, Kurume University School of Medicine, Asahi-machi, Kurume, Fukuoka, Japan
3 Executive Assistant to the President, Kurume University, Asahi-machi, Kurume, Japan
4 Department of Economics, Kyushu International University, Hirano, Yahatahigashi-ku, Kitakyushu, Japan

Corresponding Author: Yumiko Nagao, e-mail: nagaoyu@cc.saga-u.ac.jp

Source of support: This study was supported in part by a Grant-in-Aid for Scientific Research (C) (No. 25463274) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan

Background: The annual death rate from hepatocellular carcinoma (HCC) exceeds 30 000 in Japan and social control measures are urgently needed. It is important to impart knowledge about the condition and the latest therapies for viral hepatitis by holding educational seminars for affected patients. However, there are few reports indicating the impact of education on patients with liver disease. The aim of this study was to investigate the awareness and to survey the behavior of participants to whom medical information was offered in the seminar.

Material/Methods: We sent a questionnaire to 130 representative enrollees (from a total of 178) who participated in the 23rd seminar. The questionnaire addressed the following: background, knowledge, aggressiveness, information gathering, conversation, anxiety, willingness to challenge, power of communication, trust in the seminar lecturer, feeling of happiness, and continued participation.

Results: We collected information from 119 of 130 individuals (91.5%) on an anonymous basis through a postal survey; of these, 98 had liver disease (group A) and 21 had no liver disease (group B). Significant differences between the groups were the number of times of participation, age, knowledge of liver disease, willingness to challenge new treatments after participating in the seminar, and the power of communication. According to multivariate analysis, 5 factors were associated with attending more than 5 seminars: knowledge of extrahepatic manifestations, age 60 years or older, feeling of happiness from participating in the seminar, improved ability to access information about liver disease after participating in the seminar, and increased conversation about the liver disease after participating in the seminar. The adjusted odds ratios for these 5 factors were 13.94, 9.54, 7.74, 6.29, and 5.43, respectively, and each was statistically significant.

Conclusions: Repeated participation in the seminars led to increased knowledge and active behavior regarding liver disease. This approach should be effective for problem solving regarding the medical treatment of patients with a greater understanding of their disease.

MeSH Keywords: **Hepacivirus • Hepatitis B virus • Interferons • Patient Education Handout**

Abbreviations: **HCV** – hepatitis C virus; **HBV** – hepatitis B virus; **CH-C** – chronic hepatitis C; **LC-C** – liver cirrhosis type C; **CH-B** – chronic hepatitis B; **LC-B** – liver cirrhosis type B; **HCC** – hepatocellular carcinoma; **IFN** – interferon; **DAA** – direct-acting antiviral

Full-text PDF: <http://medscitechnol.com/abstract/index/idArt/896508>

 2045  3  —  19



Background

Hepatitis C virus (HCV) infection is one of the most common infections in Japan. Approximately 1.5 to 2 million people are living with hepatitis C and about 35 000 deaths are reported each year in our country [1]. In addition to interferon (IFN), many new therapies are in development for chronic hepatitis C, including direct-acting antiviral drugs (DAAs) that target specific HCV enzymes. However, because many people are unaware that they are infected, carriers may develop liver cirrhosis and hepatocellular carcinoma (HCC) and this poses a serious problem.

We previously reported on factors interfering with the acceptance of IFN therapy by HCV-infected patients at 8 facilities (clinics and hospitals) in a town in northern Kyusyu, Japan, where the prevalence of HCV infection is the highest in the country [2,3]. Multivariate analysis demonstrated that treatment facilities, sex, and the presence or absence of complications were factors associated with the risk that patients would refuse IFN therapy [3]. The evidence obtained in these studies reflected the influence of the designated requirements, effective beginning in 2009, for specialized medical institutions for liver disease in Fukuoka prefecture. We also analyzed factors motivating the acceptance of IFN therapy by 94 HCV-infected patients and showed the importance of the effort and the strength of the explanations or recommendations given by physicians to the patients [4].

In accordance with the results of our research, we have been holding regional seminars, so-called "Seminars for Digestive Disease", since October 2005. The aim of these seminars is to offer accurate medical information about liver disease and extrahepatic manifestations to help patients and their families understand their diseases, thereby facilitating their active involvement in treatment. The program provided information about HCV infection, hepatitis B virus (HBV) infection, HCC, liver treatment, extrahepatic manifestations, nutrition, and lifestyle for people with liver diseases. The seminars were led by gastroenterologists, hepatologists, and a dentist and involved other professionals, including nurses and nutritionists.

In this study, we investigated the awareness and surveyed the behavior of participants to whom medical information was offered in seminars for digestive disease.

Material and Methods

Subjects

We mailed the program of the 23rd Seminar for Digestive Disease held on July 26, 2014 to 1106 representative enrollees

who had previously participated in at least 1 seminar, from the first seminar in October 2005 to the 22nd seminar in February 2014. Out of a total of 178 respondents, 130 representative enrollees participated in the 23rd seminar (50 men, 80 women). The number seminars attended were: 1 (n=23), 2 (n=32), 3 (n=8), 4 (n=13), 5 (n=7), 6 (n=8), 7 (n=4), 8 (n=8), 9 (n=8), 10 (n=8), 11 (n=4), 12 (n=1), 13 (n=1), 14 (n=3), 15 (n=0), 16 (n=1), and 17 (n=1).

Method

Soon after the seminar, we sent a questionnaire to 130 people and collected anonymously using the postal survey method. The list of questions is given in Table 1.

Ethical considerations

This investigation was undertaken with the understanding and consent of each participant and was conducted in full accordance with the ethics principles of the World Medical Association Declaration of Helsinki. The Ethics Committee of Kurume University concluded that this study was not covered by the ethics guidelines because it was an anonymous survey.

Statistical analysis

All data are expressed as mean \pm standard error. Differences between 2 groups were analyzed using the Mann-Whitney U test, Wilcoxon's test, and Fisher's exact test. Differences were deemed significant at $p < 0.05$ (2-tailed). Adjusted odds ratios were calculated using logistic regression analysis. All statistical analyses were conducted using JMP Version 11.1.1 software (SAS Institute, Cary, NC, USA). The level of statistical significance was defined as $p < 0.05$.

Results

Characteristics of the 130 subjects

We collected the questionnaires from 119 of the 130 individuals (91.5%, 46 men and 73 women). Of these 119 respondents, 98 had liver disease (group A), and 21 did not have liver disease (group B).

The liver diseases included: chronic hepatitis C (CH-C) or liver cirrhosis type C (LC-C) (n=46, 46.9%); CH-C post-IFN (sustained virological response, SVR) (n=16, 16.3%); chronic hepatitis B (CH-B); liver cirrhosis type B (LC-B) or asymptomatic HBV carrier (n=11, 11.2%); HCV-related HCC (n=9, 9.2%); CH-C or LC-C and other liver diseases (autoimmune hepatitis, fatty liver, or alcoholic liver disease) (n=3, 3.1%); post-HCV-related HCC with post-IFN SVR (n=2, 2.0%); HCV and HBV liver disease

Table 1. List of questions sent to 130 people.

Subjects' background	Subjects' attributes (age, sex)
	Diagnosis of liver diseases (Yes, No)
Knowledge	Release of the DAA in Japan (Yes, No)
	Coffee intake and hepatocellular carcinoma (HCC) risk (Yes, No)
	<i>Vibrio vulnificus</i> infection from raw seafood (Yes, No)
	Extrahepatic manifestations (such as oral lichen planus) (Yes, No)
Desire to fight the disease by the participation in the seminar	Fight against liver disease before or after seminar participation
Information gathering	Awareness of information (books, television), before or after seminar participation
Quantity of the conversation	Increase of the quantity of conversation before or after seminar participation
Sense of anxiety regarding the liver disease	Decrease of sense of anxiety before or after seminar participation
Will to challenge the therapy	Will to challenge new treatments before or after seminar participation
Power of communication	Increase of power of communication with the family doctor before or after seminar participation
Trust in the seminar lecturers	Increase of trust in the seminar lecturer before or after seminar participation
Trust in a family doctor	Increase of trust in a family doctor before or after seminar participation
Feeling of happiness during the seminar	Fun/If anything, fun
Continued participation in the seminar	Hope through participation/If anything, hope through participation
Comments (write what you think about liver diseases)	

(CH-C or LC-C and CH-B or LC-B or asymptomatic HBV carrier) (n=2, 2.0%); post-HCC (n=2, 2.0%); HBV-related HCC and CH-B or LC-B (n=1, 1.0%); post-HCC and other liver disease (n=1, 1.0%); and other liver disease (n=5, 5.1%)

Univariate analysis

We compared the characteristics of groups A and B. The characteristics of the 130 subjects are shown in Table 2. Significant factors were: the number of seminars attended (more than 4, or 6, or 7), age (50 years or older, or 60 years or older), knowledge of liver disease (release of the DAA in Japan or *Vibrio vulnificus* infection from raw seafood), willingness to challenge new treatments after participating in the seminar, the power of communication (increase in the power of communication with the family doctor after participating in the seminar, or decrease in the power of communication with the family doctor from an earlier time).

Multivariate analysis

All variables in the univariate analyses were included in the multivariate analysis (Table 3). According to multivariate analysis, 5 factors were significant: knowledge of extrahepatic

manifestations, age 60 years or older, feeling of happiness from participation in the seminar, awareness of information gathering about liver disease after participating in the seminar, and increased conversation about liver disease after participating in the seminar. The adjusted odds ratios for these 5 factors were 13.94, 9.54, 7.74, 6.29, and 5.43, respectively, and each was statistically significant.

Discussion

Bandura advanced a theory of self-efficacy according to which personal self-efficacy is an important factor in behavior [5]. Self-efficacy is an important factor influencing an individuals' management of chronic conditions such as alcohol consumption [6], smoking cessation [7], medication adherence [8], physical activity in diabetes [9], and rehabilitation following hospitalization [10].

In patients with hypertension and type 2 diabetes, patient education has been reported to improve the state of the chronic disease [11,12]. Roumie et al. demonstrated that a multifactorial intervention including patient education improved blood pressure control compared to provider education alone [11].

Table 2. Results of univariate analysis. Comparison of 98 individuals with liver disease and 21 without liver disease among those who participated in the seminar.

		With liver disease n=98		Without liver disease n=21		P value
Sex	Male / Female	34/64		12/9		0.0552
Number of times of participation	First time	14	14.3%	6	28.6%	NS
	More than twice	84	85.7%	15	71.4%	NS
	More than three times	62	63.3%	9	42.9%	NS
	More than four times	57	58.2%	7	33.3%	0.0383
	More than five times	46	46.9%	5	23.8%	0.0519
	More than six times	42	42.9%	4	19.0%	0.0420
	More than seven times	36	36.7%	3	14.3%	0.0467
	More than eight times	32	32.7%	3	14.3%	NS
	More than nine times	24	24.5%	3	14.3%	NS
	More than ten times	17	17.3%	2	9.5%	NS
Age*	50 years old or older	95	97.9%	13	61.9%	<0.0001
	60 years old or older	84	86.6%	11	52.4%	0.0003
	70 years old or older	48	49.5%	8	38.1%	NS
	80 years old or older	10	10.3%	1	4.8%	NS
Knowledge	Release of DAAs in Japan	58	59.2%	6	28.6%	0.0107
	Coffee intake and hepatocellular carcinoma (HCC) risk	73	74.5%	12	57.1%	NS
	Vibrio vulnificus infection from raw seafood	80	81.6%	12	57.1%	0.0150
	Extrahepatic manifestations	70	71.4%	11	52.4%	NS
Willingness to fight the disease	Fight against liver disease after seminar participation	60	61.2%	14	66.7%	NS
	Fight against liver disease before seminar participation	34	34.7%	5	23.8%	NS
Information gathering	Awareness of information gathering, after seminar participation	53	54.1%	11	52.4%	NS
	Awareness of information gathering, before seminar participation	43	43.9%	8	38.1%	NS
Quantity of the conversation	Increase of the quantity of conversation after seminar participation	53	54.1%	9	42.9%	NS
	Increase of the quantity of conversation before seminar participation	37	37.8%	9	42.9%	NS
	No conversation originally	7	7.1%	3	14.3%	NS
Sense of anxiety regarding the liver disease	Decrease of sense of anxiety after seminar participation	65	66.3%	15	71.4%	NS
	Decrease of sense of anxiety before seminar participation	29	29.6%	5	23.8%	NS
	No feeling of anxiety originally	1	1.0%	1	4.8%	NS

Table 2 continued. Results of univariate analysis. Comparison of 98 individuals with liver disease and 21 without liver disease among those who participated in the seminar.

		With liver disease n=98		Without liver disease n=21		P value
Will to challenge the therapy	Will to challenge new treatment after seminar participation	40	40.8%	15	71.4%	0.0107
	Will to challenge new treatment before seminar participation	26	26.5%	6	28.6%	NS
	No will to challenge originally	3	3.1%	0	0.0%	NS
Power of communication	Increase in power of communication with the family doctor after seminar participation	50	51.0%	2	9.5%	0.0005
	Increase in power of communication with the family doctor before seminar participation	23	23.5%	5	23.8%	NS
	No power of communication with the family doctor originally	8	8.2%	14	66.7%	<0.0001
Trust in the seminar lecturer	Increase in trust in the seminar lecturer after seminar participation	74	75.5%	16	76.2%	NS
	Increase in trust in the seminar lecturer before seminar participation	22	22.4%	5	23.8%	NS
Trust in a family doctor	Increase in trust in a family doctor after seminar participation	35	35.7%	11	52.4%	NS
	Increase in trust in a family doctor before seminar participation	42	42.9%	6	28.6%	NS
	Lack of feeling of trust in a family doctor	4	4.1%	3	14.3%	NS
Feeling of happiness during the seminar	Fun	55	56.1%	13	61.9%	NS
	Fun, and/or if anything, fun	88	89.8%	19	90.5%	NS
Continued participation in the seminar	Hope through participation	84	85.7%	16	76.2%	NS
	Hope through participation and/or if anything, hope through participation	95	96.9%	20	95.2%	NS

* Blanks answer (one) is excluded

Table 3. Results of the multivariate analysis. Factors which have an influence on 98 people with liver disease who participated in the seminar more than five times.

	Odds ratio	95% CI	P value
Knowledge of extrahepatic manifestations	13.94	[3.65,68.63]	<0.0001
60 years old or older	9.54	[1.71, 68.88]	0.0090
Feeling of happiness through participation in the seminar (“fun” or “if anything, fun”)	7.74	[1.12, 77.25]	0.0372
Improvement of awareness of information gathering about liver disease	6.29	[2.10, 21.13]	0.0009
Increase in the quantity of conversation about liver disease	5.43	[1.70, 19.84]	0.0038

A meta-analysis by Gillies showed that intervention can reduce the risk of type 2 diabetes in people with impaired glucose tolerance, and lifestyle interventions seem to be at least as effective as pharmacological interventions [12]. Shah et al. reviewed the effectiveness of patient education interventions in HBV and HCV through an analysis of 14 studies [13]. They concluded that the educational interventions achieved significant improvements in patient knowledge about disease, behavior (including testing and vaccination), willingness to start and adhere to treatment, and other outcomes such as self-efficacy and vitality or energy scores. They reported that patient education interventions that teach about HBV and HCV risk factors and transmission modalities, prevention strategies including vaccination, disease testing, treatment options and adverse effects, and the natural history of the disease all seem to significantly benefit those at risk of, or diagnosed with, HBV or HCV.

In Japan there are few reports regarding the impact of education of patients with liver disease on their awareness and behavior. In our study, repeated participation in the seminar series led to increased knowledge and active behavior regarding liver disease. It is not known whether intervention through patient education on liver disease decreased the rate of development of HCC, but patient education can indirectly increase the effect of treatment and quality of life through acquiring new knowledge and improved self-determination about a definite problem in their everyday lives.

Katayama et al. reported the need to develop an effective method for the education of patients with liver disease [14]. In their report, medical staff (55 individuals) and out-patients (176 individuals) from 22 hospitals in Osaka were asked to respond to questionnaires about educational classes on liver disease. The classes were held regularly in 7 of the hospitals but not in the other 15. They reported that 95% of the medical staff and 94% of the patients thought the classes would be useful for self-management, promotion of active acceptance of treatment, and reduction of anxiety.

In our previous study, we sent questionnaires to 254 pairs of HCV carriers and their attending physicians in various areas of Japan, and we discussed the future state of medical care, in which IFN therapy would be used more widely [2]. Stratified analyses of the physicians' answers by the type of institution showed that 78.2% of liver specialists ("Hospital") gave a history of patients receiving IFN therapy, while only 15.7% of non liver-specialists ("Clinic") gave a history of patients receiving IFN therapy. Furthermore, the proportions of patients who had received an explanation about IFN therapy at the hospital and at the clinics were 88.1% and 43.1%, respectively. Similarly, IFN therapy was recommended to 90.1% of the "Hospital Patients" but only 38.6% of the "Clinic Patients" had been recommended IFN therapy by their physicians. It is important for physicians

to make greater efforts at increasing patient understanding of the therapy with accurate, easy-to-understand explanations, and to recommend the treatment to the patients; that is, the quality of communication between physicians and patients needs improvement [2].

HCV infection is associated with various extrahepatic manifestations, including mixed cryoglobulinemia, membranoproliferative glomerulonephritis, and lichen planus [15]. However, knowledge about these extrahepatic manifestations is not necessarily adequate, even in healthcare workers. When we investigated the awareness of extrahepatic manifestations in a particular Japanese medical association, 1 in 4 physicians was not aware of the extrahepatic manifestations [16].

Vibrio vulnificus infection has been correlated with pre-existing liver disease, particularly liver cirrhosis [17]. We assessed knowledge about *Vibrio vulnificus* infection in 1336 patients with chronic liver disease at 14 medical institutes in Japan [18]. Only 14.5% (194/1336) of patients had knowledge of *Vibrio vulnificus* infection. Moreover, the awareness of *Vibrio vulnificus* infections among Japanese physicians is reported to be low [19].

We analyzed the factors motivating the acceptance of IFN therapy in a total of 94 HCV-infected Japanese patients [4]. Gathering medical information from various sources led to acceptance of IFN therapy: reading a newspaper, book, or pamphlet (43.62%); watching a TV program (29.79%); watching TV reports of lawsuits over hepatitis (24.47%); participation in seminars for patients with digestive disease (22.34%); and gathering information from the internet (22.34%). Our previous study showed that the most important motivator for patients to accept IFN therapy was recommendation and encouragement from a physician, such as a primary care doctor, rather than economic reasons. Patients gathered information about liver disease and then accepted IFN therapy when they were satisfied with the explanations from their doctors.

For many years the standard treatment for hepatitis C has been IFN, which causes significant adverse effects. Recently, the treatment of HCV infection has been greatly advanced with the introduction of DAAs. In Japan, daclatasvir (DCV), asunaprevir (ASV), sofosbuvir (SFV), and ledipasvir (LDV) were launched as the first IFN-free DAAs. Clinician should continually assess how well patients understand information about their disease.

Conclusions

People who participated in more than 5 seminars had improved knowledge of liver disease as well as increased awareness and health-promoting behavior. This may be attributed to the increased self-efficacy of the patients in dealing with liver

disease. Patients who acquire power to discover self-discipline through their education will be effective in problem solving in their medical treatment; therefore, we need more creative ways to educate patients.

Competing interests

Dr. Nagao belongs to a Department funded by Nishinohon Hospital.

Acknowledgments

We thank our volunteers who helped organize the seminars: Dr. Ayato Murata (Juntendo Shizuoka Hospital), and Dr.

Tomonori Chikasue, Mr. Hiroyuki Miyazaki, Mr. Yu Imada, Mr. Junya Furusho, Mr. Kazuki Tsunoda, Mr. Ryo Shimauchi, Mr. Junjirou Rikitake, Ms. Yuki Hayashi, Ms. Akiko Kawaji, Ms. Ikumi Idera, Ms. Ayano Okawa, Ms. Misaki Tanaka, Ms. Rino Niou, Mr. Isamu Suzuki, Mr. Kousho Nishimura, Mr. Yoshihiko Otsuji, Ms. Mako Okumoto, Ms. Yuna Furuta, Ms. Yuka Watanabe, Ms. Yuki Nakao, Ms. Rikako Kobayashi (Kurume University), Ms. Anna Nakamura, Ms. Kanae Kimura (Saga Medical School), Dr. Kazumi Yamasaki (Nagasaki Medical Center), and Mr. Akihiko Matsuo, Ms. Shiori Noda, Mr. Hitoshi Noda, Mr. Daichi Inoue, Ms. Mako Iwashita, Ms. Chikako Sonoda, Mr. Yuya Sugita, Ms. Kaori Ohono (Brand-new a-cappella Society; Bas)

References:

1. Umemura T, Ichijo T, Yoshizawa K et al: Epidemiology of hepatocellular carcinoma in Japan. *J Gastroenterol*, 2009; 44(Suppl.19): 102–7
2. Nagao Y, Sata M, Suzuki F et al: Toward more widespread use of novel drug therapies – Current status of interferon therapy in patients with hepatitis C and discussion of strategies to propagate its use. Office of Pharmaceutical Industry Research. Research Paper Series, 2006; 32: 1–18
3. Nagao Y, Kawakami Y, Yoshiyama T, Sata M: Analysis of factors interfering with the acceptance of interferon therapy by HCV-infected patients. *Med Sci Monit*, 2008; 14(11): P145–52
4. Nagao Y, Sata M: Analysis of the factors motivating HCV-infected patients to accept interferon therapy. *BMC Res Notes*, 2012; 5: 470
5. Bandura A: Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev*, 1977; 84(2): 191–215
6. Christiansen M, Vik PW, Jarchow A: College student heavy drinking in social contexts versus alone. *Addict Behav*, 2002; 27(3): 393–404
7. Gwaltney CJ, Shiffman S, Paty JA et al: Using self-efficacy judgments to predict characteristics of lapses to smoking. *J Consult Clin Psychol*, 2002; 70(5): 1140–49
8. Catz SL, Kelly JA, Bogart LM et al: Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychol*, 2000; 19(2): 124–33
9. Qiu SH, Sun ZL, Cai X, Liu L, Yang B: Improving patients' adherence to physical activity in diabetes mellitus: a review. *Diabetes Metab J*, 2012; 36(1): 1–5
10. Engel C, Hamilton NA, Potter PT, Zutra AJ: Impact of two types of expectancy on recovery from total knee replacement surgery (TKR) in adults with osteoarthritis. *Behav Med*, 2004; 30(3): 113–23
11. Roumie CL, Elasy TA, Greevy R et al: Improving blood pressure control through provider education, provider alerts, and patient education: a cluster randomized trial. *Ann Intern Med*, 2006; 145(3): 165–75
12. Gillies CL, Abrams KR, Lambert PC et al: Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ*, 2007; 334(7588): 299
13. Shah HA, Abu-Amara M: Education provides significant benefits to patients with hepatitis B virus or hepatitis C virus infection: a systematic review. *Clin Gastroenterol Hepatol*, 2013; 11(8): 922–33
14. Katayama K, Yamaguchi A, Kato M et al: Viewpoints on the providing of information about liver disease to patients with chronic liver disease in classes on liver disease. *Kanzo*, 2009, 50: 356–61
15. Gumber SC, Chopra S: Hepatitis C: a multifaceted disease. Review of extra-hepatic manifestations. *Ann Intern Med*, 1995; 123(8): 615–20
16. Nagao Y, Sata M: The clinical front of hepatitis C. Strategy for the spread of IFN treatment. *Kantansui*, 2010, 61: 28–35
17. Haq SM, Dayal HH: Chronic liver disease and consumption of raw oysters: a potentially lethal combination – a review of *Vibrio vulnificus* septicemia. *Am J Gastroenterol*, 2005; 100(5): 1195–99
18. Nagao Y, Matsuoka H, Seike M et al: Knowledge of *Vibrio vulnificus* infection among Japanese patients with liver diseases: a prospective multicenter study. *Med Sci Monit*, 2009; 15(10): PH115–20
19. Osaka K, Komatsuzaki M, Takahashi H et al: *Vibrio vulnificus* septicemia in Japan: An estimated number of infections and physicians' knowledge of the syndrome. *Epidemiol Infect*, 2004; 132(5): 993–96