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FACTORS AFFECTING HIV-INFECTED PATIENTS' DECISION IN CLINICAL TRIAL PARTICIPATION

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Abstract

The numbers of clinical trials are increasing dramatically in Asia due to several reasons; large population size, potential market for pharmaceutical products and cost saving. Thailand is the first rank in the numbers of clinical trial studies in comparison with other countries in Southeast Asia. Many researchers have been discovering the reasons why some patients decide to participate in the trial; but, there is no enough evidence that such a query has been studied in the Thai population.

This research is to identify factors affecting the decision of HIV-infected patients to participate in clinical trial by using the health belief model. A structured questionnaire was developed in accordance with the six major variables in the health belief model. The questionnaire consists of respondents' characteristics, and decision to participate in the trial. Logistic regression analysis was used to identify factors affecting the decision to participate in the trial.

There were 280 patients aged between 18 – 60 years with asymptomatic HIV infection who presented at Ramathibodi Hospital, Bangkok, Thailand during May to July 2013 responded the questionnaire. About 76.4% of the respondents decided to join the clinical trial study; whereas 23.6% refused to join. The logistic regression results show that education, perceived susceptibility (*OR:* 1.579, *CI:* 1.203 – 2.074), perceived benefits (*OR* = 1.422, *CI:* 1.227 – 1.647), perceived barriers (*OR* = 0.916, *CI:* 0.852 – 0.984) and self-efficacy (*OR* = 1.496, *CI:* 1.281 – 1.747) are the key factors that affect clinical trial participation.

Results reveal that education level of HIV-infected patients is an important factor in considering their susceptibility to disease, benefits and barriers, and confidence to comply with the requirements in order to make decision to join the clinical trial study. It is recommended for future research to study further in other therapeutic diseases or areas in Thailand.

Keywords: clinical trial participation, HIV, the health belief model

Introduction

Currently, drug development industry is expanding globally. The number of industry-sponsored clinical trials has been widely spreading from North America and Europe to Asia. Data as of June 2012, 20,897 (11.23%) clinical trials in Asian countries have been registered. About 1,095 studies (32.37%) have been initiated in Thailand followed by Singapore, Philippines and Malaysia.The major therapeutic areas conducting in Southeast Asian countries are oncology and hematology followed by cardiovascular diseases except Thailand where Infectious Diseases especially HIV is the second rank[(1)]. Data as of February 19, 2013, total of 161 HIV related clinical studies including active, recruiting, terminated and completed studies and excluding unknown status were registered in clinicaltrials.gov[(2)].

Compared to developed countries, one of the significant issues is to ensure that trial subjects are recruited in compliance with Good Clinical Practice (GCP). The rights, safety and well-being of trial subjects must be protected. Illiteracy, poverty, and inadequate healthcare system in developing countries; however, can lead trial participants become vulnerable subjects. Some trial participants do not aware about their rights to freely make a decision to join in clinical trials as the connection between patients and physicians in developing countries are more paternalistic[3]. Moreover, when consider HIV-infected patients, it is not too difficult for them to access for Anti-Retroviral Therapy (ARV) in Thailand. It is more likely that these patients are motivated by some factors to be the trial subjects for new treatments. Many researchers have been discovering what motivates the patients to decide to participate in clinical trials both in developed and developing countries [4-16].

The result studied by Lovato (1997) showed that the motivating factors and barriers are varied in particular population that means Thai population might have different results from other population[9]. Exploring factors related to clinical trial participation and examining its relationship will give several benefits to investigators and the patients themselves.

Methodology

Total of 42 items were designed and developed in compliance with the health belief model. A questionnaire consists of seven (7) items of respondents' characteristics (age, gender, marital status, occupation, monthly income, education and health insurance coverage), four (4) items of perceived susceptibility, four (4) items of perceived severity, six (6) items of perceived benefits, eleven (11) items of perceived barriers, four (4) items of cues to action, five (5) items of self-efficacy, and one (1) item of clinical trial participation. The variables in the health belief model were measured by Likert's four (4) points rating scale (strongly disagree, disagree, agree, and strongly agree). Sum score of each construct of the health belief model was calculated and used for logistic regression analysis. The definition and concepts of each construct of the health belief model were adapted from Verheggen (1998) and Gorkin (1996)[12, 15].

Contents of the questionnaire were reviewed by three (3) experts for its completeness and clarity of the language. The questionnaire was validated by Content Validity Index (CVI). The questions which have CVI < 0.80 were reconsidered and adjusted. Pilot testing was done with 30 HIV-infected patients presented at Ramathibodi Hospital in May 2013. The Cronbach's alpha of perceived susceptibility (0.906), perceived severity (0.705), perceived benefits (0.919), perceived barriers (0.751), cues to action (0.745), and self-efficacy (0.930).

The research was approved by the Ethical Review Committee for Human Research before implementation. The informed consent process was conducted in compliance with ethics committee requirements for all respondents.

About of 280 adult HIV-infected patients registered at Ramathibodi Hospital during May to July 2013 were enrolled in this study. Only patients age in between 18 – 60 years old who have been receiving antiretroviral therapy, consented and able to complete the questionnaire were recruited. Patients who required hospitalization or immediate treatments, experienced to participate in the clinical trial provided investigational products and having active AIDS defining illness as defined by CDC classification were excluded.

Results

Characteristics of survey respondents

Descriptive analysis and cross-tabulation with chi-square analysis were computed to present frequency and to compare the respondents' characteristics with clinical trial participation. The overall result reveals that approximately 76.4% of respondents intended to participate in the clinical trial.

Table 1. Bivariate of correlation analysis of the association of respondents' characteristics and clinical trial participation.

		Frequency (%)	Clinical Trial Participation		*p*
			Non-Participation (%)	Participation (%)	
Total		**280**	**66 (23.6%)**	**214 (76.4%)**	
Gender					0.073
	Male	150 (53.6%)	29 (19.3%)	121 (80.7%)	
	Female	130 (46.4%)	37 (28.5%)	93 (71.5%)	
Age (years old)					0.197
	18 – 30	40 (14.3%)	14 (35.0%)	26 (65.0%)	
	31 – 40	97 (34.6%)	19 (19.6%)	78 (80.4%)	
	41 – 50	108 (38.6%)	27 (25.0%)	81 (75.0%)	
	51 – 60	35 (12.5%)	6 (17.1%)	29 (82.9%)	
Marital status					0.493
	Single	113 (40.4%)	28 (24.8%)	85 (75.2%)	
	Married	117 (41.8%)	30 (25.6%)	87 (74.4%)	
	Divorced	25 (8.9%)	3 (12.0%)	22 (10.3%)	
	Widowed	25 (8.9%)	5 (20.0%)	20 (80.0%)	
Highest education					0.424
	Junior High School or lower	89 (31.8%)	16 (18.0%)	73 (82.0%)	
	Senior High School/ Vocational	68 (24.3%)	16 (23.5%)	52 (76.5%)	
	High Vocational/Diploma	30 (10.7%)	9 (30.0%)	21 (70.0%)	
	Bachelor Degree or Higher	93 (33.2%)	25 (26.9%)	68 (73.1%)	
Monthly income (THB)					0.293
	≤ 10,000 THB	102 (36.4%)	19 (18.6%)	83 (81.4%)	
	10,001 – 20,000 THB	104 (37.1%)	24 (23.1%)	80 (76.9%)	
	20,001 – 30,000 THB	51 (18.2%)	16 (31.4%)	35 (68.6%)	
	30,001 or more	23 (8.2%)	7 (30.4%)	16 (69.6%)	
Occupation					0.210
	Government Officers	64 (22.9%)	15 (23.4%)	49 (76.6%)	
	Business Employees	46 (16.4%)	16 (34.8%)	30 (65.2%)	
	Business Owner	101 (36.1%)	24 (23.8%)	77 (76.2%)	
	Farmers	10 (3.6%)	3 (30.0%)	7 (70.0%)	
	Unemployed	37 (13.2%)	4 (10.8%)	33 (89.2%)	
	Others	22 (7.9%)	4 (18.2%)	18 (81.8%)	
Health insurance coverage					0.433
	No	99 (35.4%)	26 (26.3%)	73 (73.7%)	
	Yes	181 (64.6%)	40 (22.1%)	141 (77.9%)	

The proportions of male and female respondents were quite similar; 53.6% (male) and 46.4% (female). A majority of respondents in this research age in between 31 – 40 years old (34.6%) and 41 – 50 years old (38.6%). Only 14.3% were in between 18 – 30 years and 12.5% were in between 51 – 60 years of age. Most respondents in this research were married (41.8%) and single (40.4%). Only 8.9% of total respondents were getting divorced and widowed. Respondents mainly educated from junior high school or lower (31.8%) and bachelor degree or higher (33.2%). Approximately 24.3% educated from senior high school or vocational certificate and 10.7% from vocational certificate or diploma. About 36.4% of respondents earned less than or equal to 10,000 THB and 37.1% earned in between 10,001 – 20,000 THB; whereas 18.2% earned in between 20,000 – 30,000 THB and 8.2% earned more than 30,001 THB per month. Most respondents enrolled in this research were business owners (36.1%), government officers (22.9%), business employees (16.4%), and unemployed (13.2%). Only 3.6% were agriculturist and 7.9% were freelance and other occupations. Approximately 64.6% had medical insurance coverage by both public and private insurance schemes to pay for their medications including Civil Servant Medical Benefit Scheme (CSMBS), Universal Coverage (UC) and Social Security Scheme (SSS); however some respondents had to pay out-of-pocket (OOP) for their medications about 35.4%.

Cross-tabulation with chi-square analysis was computed to compare the respondents' general characteristics with clinical trial participation. Approximately 76.4% of respondents intended to participate in the clinical trial. The results reveal that there was no significant association among each group of respondents' general characteristics and clinical trial participation (p>0.05) as shown in table 1.

Characteristics of variables in the health belief model

Six (6) constructs of the health belief model were measured by asking relevant questions in the questionnaire with four (4) points Likert's scale. There were significant variations among each of the health belief model variables score as seen in table 2.

The mean score of variables in the health belief model; perceived susceptibility (M = 5.39, *SD* = 1.57), perceived severity (*M*= *8*.98, *SD* = 2.98), perceived benefits (*M* = 18.56, *SD* = 3.09, perceived barriers (*M* = 24.06, *SD* = 5.73), cues to action (*M* = 12.75, *SD* = 2.50), self-efficacy (*M* = 15.53, *SD* =2.94).

Table 2. Descriptive analysis of variables in the health belief model

	N	**Mean**	**SD**	**Min**	**Max**	**Items**
Perceived Susceptibility	279	5.39	1.57	4	12	4
Perceived Severity	271	8.98	2.98	4	16	4
Perceived Benefits	271	18.56	3.09	7	24	6
Perceived Barriers	267	24.06	5.73	11	38	11
Cues to Action	276	12.75	2.50	4	16	4
Self-Efficacy	277	15.53	2.94	5	20	5

The correlation of variables in the health belief model

The Pearson's correlation was used to test the multicollinearity among variables in the health belief model. The result in table 3 shows that the correlation coefficient among six (6) constructs are quite low (p<0.05).

Table 3. Correlation matrix of variables in the health belief model.

	1	2	3	4	5	6
1. Perceived Susceptibility	1.000					
2. Perceived Severity	-0.067	1.000				
3. Perceived Benefits	-0.183**	.211**	1.000			
4. Perceived Barriers	0.103	.403**	-0.148*	1.000		
5. Cues to Action	-0.24**	.236**	0.068	.213**	1.000	
6. Self-Efficacy	-0.229**	.182**	.425**	-0.176**	.225**	1.000

* Correlation coefficients are significant at the 0.01 level (2-tailed)

** Correlation coefficients are significant at the 0.05 level (2-tailed)

The factors affecting the clinical trial participation

As shown in table 4, all variables were computed by forward stepwise likelihood ratio function. Only significant variables with *p*-value less than 0.05 were included in the multiple logistic regression analysis using SPSS. Variables entered into logistic regression analysis was education (p = 0.030), perceived susceptibility (p = 0.001), perceived benefits (p<0.001), perceived barriers (p = 0.016), and self-efficacy (p<0.001). Gender, marital status, age, income, occupation, perceived severity and cues to action were not significant predictors of clinical trial participation.

In comparison with junior high school or lower, the respondents who graduated from senior high school or vocational, *OR* = 0.328, *95%CI* [0.108 – 0.995]; high vocational or diploma, *OR* = 0.151, *95%CI* [0.039 – 0.590]; and bachelor degree or higher, *OR* = 0.514, *95%CI* [0.198 – 1.337]; had the likelihood not to join the clinical trial respectively. The respondents, who believe that they are susceptible to get the opportunistic infection, would prefer to join the clinical trial, *OR* =1.579, *95%CI* [1.203 – 2.074]. The respondents, who recognize that they would get benefits from being part of the clinical trial, would decide to join, *OR* = 1.422, *95%CI* [1.227 – 1.647]. The more the respondents can foresee any obstacles that might happen to them, the more they would not join the trial, *OR* = 0.916, *95%CI* [0.852 – 0.984]. The respondents who were confident in their ability to comply the study requirements would participate in the clinical trial, *OR* = 1.496, *95%CI* [1.281 – 1.747].

Perceived susceptibility

Most of the respondents strongly agreed and agreed that the compliance of antiretroviral therapy is important for postponing of getting an opportunistic infection (97.5%), following-up the health condition periodically is essential (97.1%), following-up $CD4^+$ and viral load by blood testing periodically is necessary (96.4%), and health maintenance by doing exercise regularly is important to slow-down the occurrence of opportunistic infection (98.9%).

Perceived benefits

A majority of respondents believed that they would get more physical and mental health maintenance if they decided to participate in the trial (81.7%), being in the clinical trial, the respondents can access the high level of professional care if compared with standard of care (82.5%).the investigational products provided by clinical trials are effective (84.6%), receiving free treatments provided by the clinical study (70.8%), and the study results would cause benefits to future patients (97.5%). There were approximately 56.3% did not expect to receive money or travel compensation to be a study volunteer; whereas 53.7% believe that they should receive money or travel compensation.

Table 4. Multivariate logistic regression analysis of respondents' characteristics and variables in the health belief model.

		S.E.	*p*	OR	95% CI OR	
					Lower	Upper
Education			0.041			
Senior high school or vocational	-1.114	0.566	0.049	0.328	0.108	0.995
High vocational or diploma	-1.891	0.696	0.007	0.151	0.039	0.59
Bachelor degree or higher	-0.666	0.488	0.172	0.514	0.198	1.337
Health Belief Model						
Perceived Susceptibility	0.457	0.139	0.001	1.579	1.203	2.074
Perceived Benefits	0.352	0.075	<0.001	1.422	1.227	1.647
Perceived Barriers	-0.088	0.037	0.016	0.916	0.852	0.984
Self-Efficacy	0.403	0.079	<0.001	1.496	1.281	1.747
Constant	-10.570	2.179	<0.001	0.000		

Perceived barriers

Most of respondents did not believe that study procedures such as blood collection are barriers (68.3%), participating in the trial is time-consuming (66.4%), travelling to the site is an obstacle (58.5%), providing the study staff their personal and sensitive information are a barrier to clinical trial participation (61.6%), being a volunteer is a guinea pig (53.3%), clinical trials should not test a new drug on patients (58.4%), getting any negative implications if not join (64.6%).

Some respondents believed that the risks of untested drug might be an obstacle (53.4%), participating in the clinical trial burdens their daily life (50.2%). Moreover, almost 87.1% trusted in their physicians and 97.5%. at Ramathibodi Hospital.

Self-efficacy

Almost 64.5% of respondents were confident to visit the study site as required by the study, 84.9% to have blood tests regularly, 88.9% to record any study related events such as health conditions and medications, and 86.4% to provide their confidential information as seen in table 9.

Discussion and Conclusion

Total of 280 HIV-infected patients completed the questionnaire. Approximately 76.4% decided to participate in the clinical trial at Ramathibodi Hospital, 23.6% refused. Logistic regression analysis results discover that education, perceived susceptibility, perceived benefits, perceived barriers and self-efficacy are predictors of clinical trial participation.

Almost a hundred percent of respondents were aware of their health maintenance by following-up their disease progression regularly, complying with antiretroviral therapy, and exercising. Perceived susceptibility is emerged to be an essential factor that influences patients to receive treatments as studied by Wringe (2008).[17] However, the concept of perceived susceptibility in this research is a self-assessment of the risk of getting the opportunistic infection because all patients are already infected by HIV. Since HIV infection is a chronic condition which can be controlled by antiretroviral therapy; therefore, patients usually put their efforts to avoid any disease progression such as getting opportunistic infections. So, participating in the trial that provide investigational products can be considered as an alternative treatment. Patients can decide to receive antiretroviral therapy provided by the clinical trial or by the hospital.

Patients who believe that they would get more benefits and fewer barriers, they would decide to participate in the clinical trial. This finding is consistent with other literatures that benefits

and barriers are the main factors of clinical trial participation. According to the result, the clinical trial sponsors and the investigators should weight between the benefits and risks during the clinical trial protocol design phase. Although the clinical trial itself cannot provide direct benefits to the patients but if the clinical trial results are useful for future patients, they would be willing to join the trial.

Self-efficacy is also one of factors in clinical trial participation. If the patients considered that they could follow the requirements of clinical trial such as site visit schedule, medical data recording and reporting, study procedures, and confidentiality, they would be confident to join the clinical trials. Designing the clinical study procedure that not too tough for the patients; for example, high frequency of visit schedule, too much blood collection, lots of invasive procedures, can decrease the patients' confident to follow these rules. So, a well-designed clinical trial should have the study procedures that everyone can follow easily.

Education becomes an important factor as it is an independent variable of the variable in the health belief model. Patients with higher education were less likely to participate in the trial in comparison with junior high school or lower. This finding is inconsistent with the previous research conducted by Baquet (2006) in African American and other minorities in Maryland, that respondents with higher education and knowledgeable about clinical trials were more likely to be recruited in the trial[18]. This result can be concluded that low educated patients are easy to be influenced by clinical research professionals to participate in the clinical trial due to they do not have enough knowledge to make their own decision. This paternal relationship can usually be found in developing countries including Thailand that the physicians make decision on behalf of patients. Another research studied by Garber (2007) described the results that prior research participation experience was statistically associated with the consent to participate in future HIV trials.[19] Contrary to this previous study, this research recruited only respondents who have never joined the study before, but after providing them clinical trial information, most of respondents decided to join the trial. This step might enhance the respondents' knowledge about clinical trial so that they feel more comfortable to join the trial. So, this finding suggests that educating patients about clinical trial before asking them to make decisions is a mandatory step to increase the recruitment rate.

This research is studied only in the HIV-infected population who visited Ramathibodi Hospital, Bangkok, Thailand, the results may be varied if studies in other therapeutic area of diseases or different location. Another limitation is that no new clinical trial initiated at the time of research studying. To avoid any delay in this research studying, the clinical trial participation in this research referred to the future trials that will be exist at Ramathibodi Hospital. It is recommended to conduct this research in other therapeutic area of diseases and in other location in Thailand in order that the results can fully represent to Thai patients population. The results could be further developed to improve the patient management and also increase the recruitment rate in Thai population. Moreover, identified factors could be used for doing research in ethics in Thai population.

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