Stress, but not *Helicobacter pylori*, is Associated with Peptic Ulcer Disease in a Thai Population†

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Abstract

The purpose of this study was to clarify the relation between psychological and other risk factors, notably *helicobacter pylori (H. pylori)* infection, in contributing to the occurrence of peptic ulcer (PU) disease. A retrospective case-control study was conducted at Siriraj Hospital, Bangkok from March to December 2000. Seventy endoscopically diagnosed patients with new PU or peptic perforation were compared with 70 patients with other diseases as well as blood donors control matched for age and sex. Historical risk factors, *H. pylori* Immunoglobulin G antibody (*H. pylori* IgG Ab), stress (Perceived Stress Questionnaire) and hostility (MMPI Hostility Scale) were assessed. Data were analyzed using logistic regression analysis.

The results showed that PU was associated with chronic stress (aOR 2.9, $p = 0.01$; 95% CI, 1.3-6.5) and family history of PU (aOR 2.4, $p < 0.03$; 95% CI, 1.1-5.1), with an interaction effect between stress and irregular mealtimes (aOR 4.8, $p = 0.01$; 95% CI, 1.3-16.9). The incidence rate of *H. pylori* infection in PU patients was similar to the control group (61.4% and 50.0%, respectively, OR 1.2). The authors conclude that stress and family history, not *H. pylori* infection, are important risk factors for PU in this population. This finding supports previous studies in Thailand, showing a high

prevalence of *H. pylori* in the population but a low association with PU, in contrast to developed countries. It remains to be seen whether the impact of a family history is due to genetic factors or shared life-style patterns.

Key word : *Helicobacter Pylori* Infection, Hostility, Life-Style Factors, Peptic Ulcer Disease, Stress

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In Thailand, the incidence of peptic ulcer (PU) is very high. The annual rate of perforated operative ulcer cases at the 700-bed Udon Thani Center Hospital, in the north-eastern part of Thailand, was 192 cases in 1994 (unpublished data). Recently, in 2000 at Siriraj University Hospital, Bangkok, incident rate of endoscopically diagnosed PU represented 19.44 per cent of all patients undergoing endoscopy, while there were 44 perforated peptic ulcer cases from the surgical department (unpublished data).

Despite numerous studies of PU disease, no final conclusions can be drawn on its etiology[1-6], and it is still a controversial subject[7]. The thesis of Bauer et al from 1922 about a multifactorial mechanism seems to be valid. Factors like tobacco smoking, alcohol consumption, and coffee drinking have been related to upper gastrointestinal disease. In addition, *Helicobacter pylori (H. pylori)* infection, genetic factors and familial accumulation of peptic ulcer have been postulated[5], including indirect 'genetic' markers, such as blood group O[8,9].

Furthermore, there are few studies, based on the concept that peptic ulcer is either a heterogenous disorder or has a complex multifactorial pathogenesis. Levenstein et al[10] showed the relations between psychological factors and known biologic risk factors such as serum pepsinogen I and *H. pylori* Ab titers among ulcer patients. However, it did not include a control population. The present study selected analytic research with a retrospective case-control design to measure the influence of risk factors involving psychological, behavioral, and biological factors. The methodology was designed to correct biases inherent in the methods of detecting disease, selecting the study and control groups, and controlling the quality of the data.

The present study aimed first to determine the aetiology of PU disease based on information regarding history of disease, diet, life-style, and social and psychological factors available from the cross sectional study. Secondly, the study highlighted the need for determining interaction effects among major ulcer-risk factors, especially those between behavioral or psychological risk factors and *H. pylori* infection.

METHOD

Patient population and sampling

The patient population was divided into two groups:

The case group

The case group composed of a non-random, purposive sampling. Selected cases were symptomatic patients, in whom an active gastric or duodenal ulcer was diagnosed by endoscopy or post-operative peptic perforation at Siriraj Hospital between March and December 2000. Seventy of 72 PU patients, who were approached agreed to participate, two were excluded because of extreme stress.

The control group

To ensure the equality of the patients in the control population, each PU patient was matched with one patient both in and out patients clinic, who had another disease with no history of peptic ulcer as well as blood donors. The matching variables were age (±10 years), and sex.

Instruments

The instruments used in this study included:

1) *Personal information and the life-style factors questionnaire (LFQ)*

Personal information consisted of socio-demographic characteristics:- age, sex, ethnic origin, level of education, government payment support/health insurance; income sufficiency (not enough; enough, with no savings; enough, with inadequate savings; and enough, with substantial saving); family characteristics (marital status, family life happiness); and heredity (family history of PU in first degree relatives, blood group O). Family history of PU was evaluated by the question whether the first degree relatives had ever been diagnosed with PU disease or had symptoms of PU (persistent or episodic dyspepsia, abdominal pain, vomiting, hematemesis, and/or melena). Blood group was determined by the Blood Bank Department, Siriraj Hospital.

Family history of the PU and blood group O were dichotomized with a reference category *versus* an exposure category, the reference being "no", and the exposed category being "yes".

The LFQ was developed from the existing knowledge, literature reviews, the 1974 Alameda County Study (ACS) questionnaire[11], and Dever's Life-style Factors[12] to include items specific for ulcer-related risk factors. Some items were modified to fit the culture and resources available in Thailand. A total of 33 items were generated; 14 items were personal information, and 19 items were consumption patterns (smoking, alcohol and caffeine consumption, drug use, spicy food consumption, and irregular mealtimes).

Evidence for the content validity of the LFQ came from the fact that the measure was taken from previously validated instruments for assessing health and life-style, and from actual clinical practice as well as those described in the clinical literature. These life-style factor items were submitted to 5 Thai doctorally prepared nurses with expertise in public health, epidemiology, and clinical nursing. Experts were asked to indicate whether they agreed or disagreed with the categorization of each item in the LFQ. Suggestions for additional life-style factor items and for modifications of the existing items contributed to the revision and refinement of the LFQ.

The subjects were interviewed regarding the history of ulcers in first degree relatives; any use of alcohol; total amount of cigarettes during their lifetime, daily use of coffee and spicy diet consumption before symptom onset; irregular mealtime {never, not frequent (less than once a week), rather frequent (one or two times a week), frequent (three or four times a week), and almost everyday}; and use of aspirin or other NSAIDs, or steroids, daily within two weeks before symptom onset to determine causality.

For continuous variables, the total raw scores were divided into four categorical subgroups: the first quartile score as low-score level, the second and the third quartile score as moderate-score level, and the fourth quartile score as high-score level. Subjects were then dichotomized into a reference group of subjects with scores in the lower three quartiles *versus* the exposed group with scores in the highest quartile. Thus, the reference group of smoking was identified as low-score subgroup plus moderate-score subgroup (the lower three quartiles) *versus* the "exposed" high-score subgroup (the uppermost quartile).

Similarly, for alcohol and caffeine consumption, irregular mealtimes, and use of non-steroidal anti-inflammatory drugs, aspirin, or steroids, each of the reference groups was the lower three quartiles *versus* the exposed group of the uppermost quartile. For spicy food consumption, the reference group was fewer than 10 chilies per day *versus* the exposed group of over 10.

2) *The perceived stress questionnaire (PSQ)*

This 30-item, 4-point questionnaire, is a measure of stress specifically intended for clinical

psychosomatic research developed by Levenstein S, Prantera C, Varvo V, et al, in 1993[13]. The strengths of the PSQ are that it measures a final common denominator of stress, uses simple language, and is acceptable, not-intrusive, not culture-bound, relatively unaffected by disease symptoms, etc. Conversely, the limitation of the PSQ is theoretical unclarity, including a mix of such different kinds of items as distress ('calm'), outside pressures ('deadlines'), and perceptions ('afraid for the future'). The Thai PSQ version was produced using the translation- back-translation technique for accuracy of language. Each item ranged from almost never (coded 1) to usually (coded 4), Possible scores ranged from 30 to 120. Higher scores indicated a higher perceived stress.

The Thai PSQ was submitted to 5 Thai experts for content review. All experts were asked to judge the appropriateness of the translation of each item of the PSQ. As a measure of the internal consistency of the PSQ, the coefficient alpha was 0.90 among thirty peptic ulcer patients and twenty-five patients with other diseases, and was 0.91 among all 140 case and control subjects in the final sample.

The PSQ was administered using an interview, covering the year preceding diagnosis. Subjects were, again, dichotomized into a reference group of subjects with scores in the lower three quartiles *versus* an exposed group with scores in the highest quartile.

3) *The MMPI-based Cook and Medley hostility scale (Ho scale)*

A 27-item, 2-point questionnaire, developed by Cook W and Medley D[14] measures similarity to a type of individual characterized by a dislike for and distrust of others. Based upon empirical analyses of individual items and correlations with other measures of hostility, an emerging consensus has been that the Ho scale is related less to overt anger than to a combination of anger proneness and a cynical, distrusting view of others[15-17]. In addition, high Ho scores might reflect neuroticism, social difficulties, and ineffective coping as well as anger and hostility [18]. So there was consensus that the Ho scale was multidimensional, measuring different aspects of hostility as well as dysphoria. However, Barefoot, et al [19] found that the sum of three of the six categories, Cynicism, Aggressive Responding, and Hostile Affect (called the Sum Score) was more strongly predictive of survival than the Ho scale score. Therefore, the three hostility subscale measures (the Sum Score) were used in this study. It included 27 true-false items, each scores as 0 (disagree) or 1 (agree). Possible scores thus range from 0 to 27; reverse scoring was performed on item 17, 21. The higher the score, the stronger the degree of hostility.

The Minnesota Multiphasic Personality Inventory (MMPI) was first translated into Thai by Assistant Professor Kasemsak Pomsrikaew, Faculty of Educational Psychology, Chulalongkorn University, Thailand. Stability of the Ho Scale was determined by a pilot study. The reliability coefficient of this scale for fifteen case and fifteen control subjects, estimated by the coefficient alpha, was 0.78, and the KR-20, was 0.79. The reliability testing among 140 case and control subjects in the final sample yielded an Alpha Cronbach's Coefficient of 0.69. The subjects were administered the Ho scale by interview. As with other continuous variables, subjects were dichotomized into a reference group of subjects with scores in the lower three quartiles *versus* an exposed group with scores in the highest quartile.

4) *H. pylori*

The IgG Ab enzyme-linked immunosorbent assay (ELISA) serologic test. Serologic tests are the most acceptable method for detection of *H. pylori* in large epidemiologic studies, which have sensitivities of 80 per cent to 95 per cent, and specificities range from about 75 per cent to 97 per cent[20-32].

Serum of all subjects were collected and examined for *H. pylori* IgG Ab at the Department of Microbiology, Faculty of Medicine, Siriraj Hospital using the PanBio *H. pylori* IgG ELISA KIT.

H. pylori IgG Ab was divided into a reference category (antibodies negative values) *versus* an exposure category (antibodies positive values).

Data collection

The protocal was approved by the Human Subjects Committee, Siriraj Medical School Hospital. All patients were informed about the objectives of the study and gave their consent.

For the case population group, age at first ulcer and blood type, when available, were recorded. Beginning in March 2000, blood was drawn from consenting subjects for the determination of *H. pylori* IgG ELISA test (investigated by Jearanaisilavong J, Department of Microbiology, Siriraj Hospital). Within two weeks of endoscopy or operation for peptic perforation, the investigator requested the patients to

answer all of the checklist questionnaires or interviewed, regarding history of ulcer in a first degree relative, any use of alcohol, lifetime cigarette use, daily use of coffee and spicy diet before symptom onset, and use of aspirin or other NSAIDs, or steroids daily within two weeks before symptom onset to determine causality. The PU patients also answered the PSQ and the Ho scale.

The control population also was requested to answer all of the checklist questionnaires or interviewed. Blood samples were drawn for the determination of *H. pylori* IgG Ab and blood group.

RESULTS

Demographic characteristics

An endoscopically diagnosed new PU group of 70 patients which included 25 with gastric ulcer, 23 with duodenal ulcer, 2 with gastric and duodenal ulcer, 20 with perforated ulcers (12 gastric, 8 duodenal) was compared with 70 hospital-based patient controls matched for age and sex (each of 54 men, 16 women). The mean age was 47.07 ± 16.47 years in ulcer patients and 45.93 ± 15.94 years in control group. Their ages ranged from 15 to 89 years. Socioeconomic status tended to be lower in ulcer patients than in controls, but there were no significant differences in ethnicity, marital status, family income, health payment support, or educational level.

The majority of the study population (77.1%) were male, while only 22.9 per cent were female. The majority of them (66.43%) had regular incomes, while 33.57 per cent did not have a regular income secondary to retirement (15%) and unemployment (10.71%), 31.43 per cent had a monthly income of 2,001-5,000 baht which is below the poverty line (5,774 baht/month), while 25.71 per cent had a monthly income over 11,000 baht. One subject reported no family income. More than half of the subjects (61.43%) had no government payment support or health insurance, while 32.86 per cent had support (Table 1).

Of all subjects, 55.7 per cent (78 cases) were positive for *H. pylori*. Looking at the subjects according to *H. pylori* IgG Ab status, the two groups did not differ significantly in sex, educational level, income adequacy, or sleep adequacy. Being over 46 years old ($p = 0.05$) was more common among *H. pylori*-positive subjects (Table 2). These findings suggested that in this population *H. pylori* infection was affected by aging but not by socioeconomic status.

Association between major ulcer risk factors and peptic ulcer

The preliminary results used contingency tables in univariate analyses to estimate odds ratios. Peptic ulcer patients had higher values than controls on PSQ scores (OR 2.8, $p = 0.01$; 95% CI, 1.2-6.3) and family history of PU (OR 2.3, $p < 0.03$; 95% CI, 1.1-4.9) (Table 3). There was no significant association with *H. pylori* Ab positivity, or with other life-style variables.

This population had an extremely low rate of exposure to drug or NSAIDs use, thus the present study offered a unique opportunity to examine the associations between major known life-style risk factors associated with ulcer disease such as smoking, and spicy food dietary habits, alcohol and coffee consumption, drinking caffeinated beverages, stress, and personality type in a population with low exposure to medications (Table 3).

On multivariate logistic regression analyses, the backward stepwise likelihood ratio model backwardly eliminated non-significant variables step by step. At each step the -2 log likelihood, the Goodness-of-Fit, and the model chi-square were examined in order to determine the suitable model. According to Table 3, it was found that there were only two kinds of drugs used in the case group, NSAIDs ($n = 2$) and unidentified drugs ($n = 15$), and none in the control group. Because of low frequencies of drug use in this population, the fit model had higher coefficient and SE (β_i) of unidentified drugs -8.28 and 15.14 respectively. Since the standard error had higher values than the coefficient, this model was compared to a new model without unidentified drug and NSAIDs variables. Comparison between the new and the old model, revealed there was a change in Log Likelihood (from 153.65, 162.37 to 177.248, 182.545) and Improvement in Chi-Square (p-value from 0.001, 0.000 to 0.207, 0.003) (Table 4). In this case, drugs-use risk factor was considered to be excluded in the new model.

The estimated model fit to describe the probability of occurrence of peptic ulcer was determined by the final model as the log odds of peptic ulcer disease ($\text{Log}_e [P_1/(1-P_1)]$) = -0.51 + 1.05 PSQ score + 0.86 Family Hx of PU). There was statistically significant effect of PSQ score (aOR 2.9, $p = 0.01$; 95% CI, 1.3-6.5) and family history of PU (aOR 2.4, $p < 0.03$; 95% CI, 1.1-5.1).

Table 1. Frequency distribution and percentage of the case and the control groups classified by sex, age group, educational level, marital status, earned ownself, family income, government payment support/health insurance, and income adequacy (n = 140).

Demographic characteristics	Ulcer (n = 70)	%	Control (n = 70)	%	Sum (n = 140)	%	Chi-square
Age group							
15-45 years	32	45.7	32	45.7	64	45.7	0.00ns
46-70 years	34	48.6	34	48.6	68	48.6	
Over 70 years	4	05.7	4	05.7	8	05.7	
Age in years*	47.07 ± 16.47		45.93 ± 15.94				t-value = 0.42ns
Sex							
Male	54	77.10	54	77.10	108	77.10	0.00ns
Female	16	22.90	16	22.90	32	22.90	
Educational level							3.034ns
No formal education	5	7.14	2	2.86	7	5.00	
Elementary school	39	55.71	39	55.71	78	55.71	
High school (grade7-9)	11	15.71	15	21.43	26	18.57	
High school (grade10-12)	2	2.86	2	2.86	4	2.86	
Higher education	4	5.72	3	4.28	7	5.00	
Vocational school	4	5.72	7	10.00	11	7.86	
Studying now	3	4.28	2	2.86	5	3.57	
Missing value	2	2.86	0	0.00	2	1.43	
Mother's Race							2.33ns
Thai	63	90.00	63	90.00	126	90.00	
Chinese	6	8.57	5	7.14	11	7.89	
Other	1	1.43	2	2.86	3	2.14	
Marital status							1.72ns
Single	16	22.8	22	31.4	38	27.1	
Married	41	58.6	39	55.7	80	57.2	
Widow/divorced/separate	13	18.6	9	12.8	22	15.7	
Personal earning							0.20ns
Earned	44	63.0	49	70.00	93	66.43	
Out of work	9	12.80	6	08.57	15	10.71	
Retirement	12	17.08	9	12.86	21	15.00	
Housework	1	01.42	2	02.86	3	02.15	
Student	4	05.70	4	05.71	8	05.71	
Family income (baht/month)							4.48ns
0	1	1.43	0	0.00	1	0.71	
≤ 2,000	9	12.86	7	9.99	16	11.43	
2,001-5,000	26	37.14	18	25.71	44	31.43	
5,001-8,000	12	17.14	15	21.43	27	19.29	
8,001-11,000	6	8.57	10	14.29	16	11.43	
> 11,000	16	22.86	20	28.57	36	25.71	
Government payment support/ health insurance							1.20ns
No	46	65.71	40	57.14	86	61.43	
Yes	20	28.57	26	37.14	46	32.86	
Personal business	4	5.72	4	5.72	8	5.71	
Income Adequacy							5.94ns
Not enough	27	38.6	14	20	41	29.3	
Enough, with no savings	20	28.6	28	40	48	34.3	
Enough, with inadequate savings	14	20	17	24.3	31	22.1	
Enough, with substantial savings	9	12.8	11	15.7	20	14.3	

* Mean ± Standard Deviation

Table 2. Frequency distribution and percentage of groups negative and positive for HP IgG antibodies by age group, sex, educational level, income adequacy, and adequacy of sleeping time (n = 140).

Demographic characteristics	HP-Negative %	HP-Positive %	Sum (n = 140)	%	χ^2	P-value
Age group						
15-45 years	34	30	64	45.7	3.73	0.05*
> 46 years	28	48	76	54.3		
Sex						
Male	44	64	108	77.10	2.41	0.12ns
Female	18	14	32	22.90		
Educational Level						
No formal						
Education and elementary school	46	67	113	80.7	3.04	0.08ns
High school and higher education	16	11	27	19.3		
Income Adequacy						
Not enough and enough, with no saving	49	70	119	85.0	3.11	0.08ns
Enough, with inadequate savings and enough, with substantial saving	13	8	21	15.0		
Sleep Adequacy						
Enough	17	30	47	33.6	1.89	0.17ns
Not enough	45	48	93	66.4		

Comparison of odds ratios between univariate analysis and multivariate analysis among ulcer-risk factors and peptic ulceration

The comparison of odds ratios between univariate analysis and logistic regression analysis is shown in Table 3.

On logistic regression analysis peptic ulcer patients had significantly higher values than controls on PSQ score ($p = 0.01$). The result was not much different from univariate analysis ($p = 0.01$). For family history of PU as well, the result was little different from univariate ($p < 0.03$), so perceived stress and family history of PU persisted as major risk factors of peptic ulceration. As a result, the hypothetical model including family history of PU, blood group O, life-style factors (smoking, alcohol and caffeine consumption, irregular mealtime, spicy food consumption), hostility score, perceived stress score, and serum *H. pylori* IgG Ab is partially supported.

Interaction effects are shown in Table 5. It was found that there was no statistically significant interaction effect between the PSQ and *H. pylori* IgG Ab, hostility score and *H. pylori* IgG Ab, the PSQ score and Family history of PU, alcohol consumption and irregular mealtime, *H. pylori* IgG Ab and irregular mealtime, alcohol consumption and smoking, etc. The only significant interaction effect was between the PSQ score and irregular mealtime ($p = 0.01$) (Table 5).

Analyses of these cases of new PU showed that two risk factors were correlated with PU disease. Statistically significant risk estimates were found for chronic stress and for a family history of PU in the univariate analyses. The multivariate analyses showed that both of the evaluable major ulcer-risk factors (stress and family history) independently contributed to increased risk for new ulcer cases. In addition, irregular mealtimes had interaction with stress in causing ulcer.

DISCUSSION

The study results indicated that highly chronic stress measured by the PSQ score and family history of PU disease, was more common in new PU patients than in control patients. Between the two significant variables, however, there was no interaction effect. Conversely, irregular mealtimes emerged as the only variable with a power to interact with chronic stress in causing an ulcer (aOR 4.8**, $p = 0.01$; 95% CI, 1.3-6.9).

In the univariate analysis, irregular mealtimes did not appear to be a significant aetiology of PU disease (Table 3). When high stress is combined with skipping some meals, whether because of loss of appetite or otherwise, the stomach is prone to prolonged acid hypersecretion, which could induce development of an ulcer.

Table 3. Crude odds ratios by using a chi-square test, and adjusted odds ratios, by logistic regression in a complete multivariate model. Examining the association between ulcer-risk factors and the occurrence of peptic ulcer.

Variable	Control	%	Ulcer	%	CrudeOR	P-value	χ^2	Adjust OR	P-value	95% CI
PSQ										
Low to Moderate	59	84.3	46	65.7	2.8**	0.01	6.44	2.9**	0.01	1.3-6.5
High	11	15.7	24	34.3						
PU Family Hx										
No	55	78.6	43	61.4	2.3*	0.03	4.89	2.4*	0.03	1.1-5.1
Yes	15	21.4	27	38.6						
Blood group O										
No	48	68.6	41	58.6	1.54ns	0.09	4.73	1.67ns	0.17	0.8-3.5
Yes	22	31.4	29	41.4						
H. pylori IgG Ab										
Negative	35	50.0	27	38.6	1.59ns	0.17	1.85	1.30ns	0.47	0.6-2.7
Positive	35	50.0	43	61.4						
Hostility										
Low to Moderate	56	80.0	54	77.1	1.18ns	0.68	0.17	1.13ns	0.79	0.5-2.7
High	14	20.0	16	22.9						
Smoking										
Low to Moderate	61	87.2	59	84.3	1.26ns	0.23	1.45	1.74ns	0.29	0.6-4.8
High	9	12.8	11	15.7						
Drinking Alcohol										
Low to Moderate	61	87.2	57	81.4	1.55ns	0.06	3.46	1.43ns	0.50	0.5-4.1
High	9	12.8	13	18.6						
Caffeine Intake										
Low to Moderate	57	81.4	59	84.3	0.82ns	0.65	0.20	0.57ns	0.27	0.2-1.5
High	13	18.6	11	15.7						
Irregular Mealtime										
No	15	21.4	15	21.4	1.00ns	1.00	0.00	1.03ns	0.94	0.4-2.5
Yes	55	78.6	55	78.6						
Spicy diet										
Low to Moderate	56	80.0	54	77.1	1.10ns	0.68	0.17	1.01ns	0.97	0.4-2.5
High	14	20.0	16	22.9						
Unidentified drugs										
No	70	100	55	78.6	-	-	-	-	-	-
Yes	00	00.0	15	21.4						
NSAIDs										
No	70	100	68	97.1	-	-	-	-	-	-
Yes	00	00.0	2	2.9						

ns = Non significant, * p-value < 0.03, ** p-value = 0.01

Table 4. Comparisons of improvement in chi-square between the new model without drug-use variables and the old model with drug-use variables.

Backward stepwise No.	df	Term entered	Term removed	New model			Old model		
				Log likelihood	Model improvement		Log likelihood	Model improvement	
					χ^2	P-value		χ^2	P-value
1	8	All 12 variables		177.248	16.833	0.207	153.65	40.43	0.001
2	8		Age gr	177.253	16.828	0.156	153.72	40.36	0.000
3	8		Sex	177.254	16.828	0.078	153.72	40.36	0.000
4	8		Spicy	177.255	16.827	0.052	153.73	40.35	0.000
5	8		Mealtime	177.260	16.821	0.032	153.76	40.32	0.000
6	8		Hostility	177.330	16.751	0.019	153.79	40.29	0.000
7	8		Alcohol	177.775	16.306	0.012	153.85	40.23	0.000
8	8		*H. pylori* IgG	178.287	15.794	0.007	154.25	39.83	0.000
9	7		Caffeine	179.519	14.562	0.006	155.53	38.55	0.000
10	4		Smoking	180.663	13.418	0.004	156.84	37.25	0.000
11	2	PSQ, PU Family Hx	Blood gr.	182.545	11.536	0.003	158.57	35.52	0.000
12	3	PSQ, PU Family Hx, Unidentified drug					162.37	31.70	0.000

Furthermore, the study showed that PU occurred more frequently in first degree relatives of patients than in the relatives of control patients. It should be further explored whether family history of PU is primarily influenced by heredity (genetic factors), by similar life-style patterns in their families, or both, in causing PU disease. *H. pylori* IgG Ab as well as a series of historical risk factors did not seem to play a role in peptic ulceration in the present study. The frequency of blood group O, smoking, alcohol and spicy food consumption in the PU patient group was somewhat higher than the control group (Table 3).

The socioeconomic status of *H. pylori* IgG Ab-positive subjects compared to *H. pylori* IgG Ab-negative was not significantly lower, in the present study. As measured by educational level, income adequacy, or, sleep adequacy. Age over 46 years old ($p = 0.05$) was higher among *H. pylori* IgG Ab-positive patients (Table 2), supporting the concept that *H. pylori* infection can be increased by aging.

Though its discovery has revolutionized thinking about the aetiology and treatment of PU, *H. pylori* is neither a necessary nor a sufficient condition for ulcer formation: well over half of the population has been exposed to *H. pylori* by the age of 70 years[33]. Only 15 per cent of *H. pylori*–infected persons develop PU disease, suggesting that specific factors are required for ulceration to occur. Interestingly, the present finding revealed that the proportion of *H. pylori* infection in PU patients was 0.61 (43 of 70 patients), whereas the proportion of *H. pylori* infection in the control group was 0.50 (35 of 70 patients) (Table 3). That is similar to a previous study in Thailand by Kachinthon, Atisook, et al[34] finding that the overall proportion of *H. pylori* infection in a normal population was 0.497. This also supported epidemiological studies by Meyer et al[33] using serological tests shown that a large proportion of healthy people had antibodies against *H. pylori.*

The present findings resemble those of another study by Mairiang, Kositchaiwat, et al[35], who reported that the overall proportion of *H. pylori* infection in PU was 0.67 (18 of 27 patients) among 221 dyspeptic patients at Srinagarind Hospital, Khon Kaen, and Ramathibodi Hospital. Furthermore, the finding seems to support a study of *H. pylori* prevalence and eradication in Bhumibol Adulyadej Hospital between 1997-1998 which found that of a total of 282 cases the proportion of *H. pylori*-positivity was 0.51 in gastric ulcer (GU) patients and 0.65 in duodenal ulcer (DU). The authors concluded that 'preva-

Table 5. Comparison of interaction effect among ulcer-related variables.

Interaction terms	Odds Ratio	P-value	95% CI
PSQ*PU family Hx	4.01	0.12ns	0.71-22.65
PU family Hx *Sex	1.05	0.92ns	0.44-2.40
PSQ*Sex	1.46	0.46ns	0.54-3.93
H. pylori IgG Ab*PSQ	0.65	0.55ns	0.16-2.65
H. pylori IgG Ab*Ho	1.69	0.39ns	0.50-5.73
PSQ*Irregular meals	4.77	0.01**	1.35-16.88
Alcohol*PSQ	1.26	0.57ns	0.57-2.81
H. pylori IgG Ab*Irregular meal	1.37	0.42ns	0.63-2.97

ns = Non significant, * p-value = 0.05, ** p-value = 0.01

lence of *H. pylori* and PU in Thailand is not the same as in developed countries'[36]. Whilst in developed country, 90-100 per cent with DU and 70-90 per cent of those with GU had *H. pylori* infection[37-42]. It is concluded that despite strong evidence that the prevalence of *H. pylori* infection in the Thai population is higher than in developed countries[43], a lower rate of *H. pylori*-positive peptic ulcer incidence occurred. In Thailand there was a relatively low average percentage of *H. pylori* infection in PU patients in all of the above four studies (mean = 61.72%). Furthermore, a study by Suthienkul and Tanjatham[44] suggested that the pathogenic mechanisms of *H. pylori* infection have not been clearly demonstrated. Supported by Graham & Yamaoka (2000), who suggested that considering *H. pylori* infection on a global basis, the *H. pylori* strain plays a lesser role, the virulence of the strain acting primarily as an accelerator of the disease process and not as a predictor of outcome[45].

The validity of the present study depends on accurate recall by the patient. The exposure variables sought, however, are such that they are likely to be remembered. Moreover, this is an age-matched comparison, and unless it is considered that recall is less reliable in one group (which is unlikely), the error induced by faulty recall is reduced by the design. Besides, there is limitation in retrospective case-control study, cases may be more likely than the controls to recall details of their past ulcer-related risk factors.

The present study shows that neither *H. pylori* infection nor some of the other well-known historical risk factors seems to play a major role in the development of PU disease in one Thai population. Findings from the present study suggest some recommendations for future research that may be conducted based on these study results. Risks of PU need to be reexamined in other populations in order to compare and confirm the findings. Non-significant trends should also be reassessed. Either hostility or some specific personality patterns should be reinvestigated with other more specific instruments. *H. pylori* infection might be reevaluated by other non-invasive methods such as urea breath test in order to compare and confirm the findings. Furthermore, the life-style factors need to be reassessed. In particular in case of use of unidentified drugs the specific kind of drugs may be verified e.g. asking to look at a medicine bag or package when possible. In the community, it would be useful to investigate the drug stores where the patients bought the drug, e.g. asking, 'For a symptom like this, what kind of drugs would you sell to patients?' A retrospective study such as this needs to be reinvestigated in other settings of Thailand. This retrospective study was able to identify several risk factors in a relatively small sample size, obtain the results quickly, and also discover an interaction between chronic stress and irregular mealtimes. This emerging interaction, discovered by this case-control study, confirmed findings by Levenstein et al[38] that skipping breakfast was a mediator for stress.

In conclusion, this study revealed that stress was an important risk factor for development of an ulcer, and it interacted with irregular mealtimes in causing ulcer. Family history of PU was significantly and independently associated with the occurrence of peptic ulcer. The finding could support that peptic ulcer disease is not a homogeneous group of disorders despite the fact that the ulcers affect the same sites of the stomach and duodenum. There are marked differences in the pathogenetic mechanisms and genetic background between ulcer patients. This present study may be important to increase the understanding of biopsychosocial factors and a holistic viewpoint which

will ultimately enhance the effectiveness of prevention and control of this important health problem.

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ความเครียด ไม่ใช่ภาวะติดเชื้อ*เฮลิโคแบคเตอร์ ไพลอไร* มีความสัมพันธ์กับการเกิดโรคแผลในกระเพาะอาหารและลำไส้เล็ก ณ โรงพยาบาลศิริราช†

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การวิจัยครั้งนี้เป็นการวิจัยย้อนหลังแบบกลุ่มศึกษาและกลุ่มควบคุม มีวัตถุประสงค์เพื่อศึกษาปัจจัยที่มีอิทธิพลต่อการเกิดโรคแผลในกระเพาะอาหารและลำไส้เล็กหรือแผลเป็นติด ได้แก่ วิถีชีวิต บุคลิกภาพก้าวร้าว ความเครียดเรื้อรัง และภาวะติดเชื้อ*เฮลิโคแบคเตอร์ ไพลอไร* ใช้เวลาในการศึกษา 10 เดือน คือระหว่างเดือนมีนาคม ถึง เดือนธันวาคม 2543 ณ โรงพยาบาลศิริราช กลุ่มตัวอย่างจำนวน 140 ราย กลุ่มศึกษาได้แก่ ผู้ป่วยโรคแผลเป็นติดที่ได้รับการวินิจฉัยด้วยการส่องกล้องทางเดินอาหารหรือผู้ป่วยหลังผ่าตัดกระเพาะอาหารทะลุ ที่ยินดีเข้าร่วมการวิจัยจำนวน รวม 70 คน จากจำนวนทั้งสิ้น 72 คน ผู้ป่วยกลุ่มควบคุมประกอบด้วย ผู้ป่วยโรคอื่น ๆ และผู้บริจาคโลหิตรวมถึงบุคคลทั่วไปจำนวน 70 คน โดยวิธีการจับคู่เพศและอายุ เครื่องมือในการวิจัยได้แก่ แบบบันทึกข้อมูลส่วนบุคคล แบบสอบถามด้านวิถีชีวิต แบบวัดการรับรู้ความเครียดและแบบวัดบุคลิกภาพก้าวร้าว รวมทั้งการตรวจซีรัมหาแอนตีบอดีต่อเชื้อ*เฮลิโคแบคเตอร์ ไพลอไร* โดยใช้สถิติการวิเคราะห์การถดถอยพหุแบบลอจิสติก

ผลการศึกษาพบว่าปัจจัยที่มีผลต่อการเกิดโรคแผลเป็นติดได้แก่ ความเครียดเรื้อรัง (aOR 2.9, p = 0.01; 95% CI, 1.3-6.5) และประวัติบุคคลในครอบครัวป่วยด้วยโรคแผลเป็นติด (aOR 2.4, p < 0.03; 95% CI, 1.1-5.1) สอดคล้องกับผลการวิเคราะห์โดยใช้สถิติไคสแควร์ และวิถีชีวิตที่มีผลร่วม (interaction effect) กับความเครียดในการทำให้การเกิดโรคแผลเป็นติดได้แก่ การรับประทานอาหารไม่เป็นเวลา (aOR 4.8, p = 0.01; 95% CI, 1.3-16.9) ส่วนบุคลิกภาพก้าวร้าวและวิถีชีวิตที่เป็นผลลบต่อสุขภาพ ตลอดจนภาวะติดเชื้อแบคทีเรีย*เอช. ไพลอไร* ในกระเพาะอาหาร ในการวิจัยครั้งนี้ไม่พบว่ามีนัยสำคัญทางสถิติ ในการวิจัยครั้งนี้สำหรับผู้ที่มีประวัติการเจ็บป่วยโรคแผลเป็นติดในครอบครัวอาจมาจากสาเหตุทางพันธุกรรมหรือวิถีชีวิตที่คล้ายคลึงกันของบุคคลในครอบครัวเดียวกัน หรือสาเหตุร่วมกันทั้งสองประการ ซึ่งควรทำการศึกษาต่อไป อัตราอุบัติการณ์ของภาวะติดเชื้อแบคทีเรีย*เอช. ไพลอไร* ในกระเพาะอาหาร ในกลุ่มควบคุมและผู้ป่วยโรคแผลเป็นติดมีความใกล้เคียงกัน (50% และ 61.43%) โดยสนับสนุนข้อค้นพบก่อนหน้าในประเทศไทย ซึ่งแตกต่างจากข้อค้นพบในประเทศพัฒนา

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