

## Peptic ulcer and childhood adversities experienced by working-aged people

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### Abstract

**AIM:** To study the association between self-reported peptic ulcer and childhood adversities.

**METHODS:** The Health and Social Support Study (HeS-Sup) population consisted of a stratified random sample drawn from the Finnish Population Register in four age groups: 20-24, 30-34, 40-44 and 50-54. The survey was carried out by postal questionnaire during 1998, with a response rate of 40.0%. A follow-up questionnaire was sent during 2003 to all those who responded to the first. Altogether 19626 individuals returned the follow-up questionnaire; a response rate of 75.8%. The subjects were asked whether a doctor had told them that they have or have had peptic ulcer. The analyses covered those who responded affirmatively to both the baseline and the follow-up enquiries ( $n = 718$ ). Those not reporting a peptic ulcer in either of the two questionnaires ( $n = 17677$ ) were taken as controls. The subjects were further requested (through six questions) to think about their childhood adversities.

**RESULTS:** The most common adversities mentioned were long-lasting financial difficulties in the family, serious conflicts in the family, and a family member seriously or chronically ill. All the adversities reported, except parental divorce, were more common among peptic ulcer patients than among controls ( $P$  values

varied between  $< 0.001$  and  $0.003$ ). Age- and sex-adjusted odds ratios (OR) of childhood adversities in the multivariate logistic analysis for self-reported peptic ulcer varied between 1.45 and 2.01. Adjusting for smoking, heavy drinking, stress and nonsteroidal anti-inflammatory drug use had no further influence (ORs between 1.22 and 1.73).

**CONCLUSION:** Our findings suggest that childhood adversities maintain a connection with and have a predictive role in the development of peptic ulcer.

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**Key words:** Peptic ulcer; Working-aged; Childhood adversities; Stress factors; Predictive role

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### INTRODUCTION

*Helicobacter pylori* (*H. pylori*), nonsteroidal anti-inflammatory drugs (NSAID) and smoking are the most important risk factors for peptic ulcer<sup>[1]</sup>. Infection with *H. pylori* causes most duodenal ulcers (95%) and gastric ulcers (70%)<sup>[2]</sup>. Between 89% and 95% of peptic ulcer-related serious upper gastrointestinal events may be attributed to NSAID use, *H. pylori* infection and cigarette smoking. Moreover, there is synergism for the development of peptic ulcer and ulcer bleeding between *H. pylori* infection and NSAID use<sup>[3]</sup>. Alcohol intake may also play a role in the development of gastric ulcers<sup>[4]</sup>.

Between 5% and 20% of patients with gastric or duodenal ulcers lack an identifiable organic etiology<sup>[5]</sup>. Psychological stress may also have an impact on the onset and course of ulcer disease<sup>[6]</sup>. Moreover, various types of stress may play a role in the onset and modulation of acute or chronic peptic ulcer disease<sup>[7]</sup>. Persons who perceive their lives as stressful may run an increased risk of

developing peptic ulcer disease<sup>[8]</sup>. In low socioeconomic populations psychological stress and health risk behaviours contribute to an increased risk of ulcer<sup>[9]</sup>. However, familial aggregation of the disease is modest, according to a population-based twin cohort study<sup>[10]</sup>.

Childhood is an important and vulnerable period in individual development. Early life experiences are particularly important in determining how the individual responds over the life course<sup>[11]</sup>. However, very little is known as to how childhood adversities concerning financial problems, conflicts in the family, problems with alcohol, and matters of personal security are associated with peptic ulcer. We now examine this aspect in a nationwide sample in Finland, enquiring whether there has been something particular in the social circumstances of peptic ulcer patients during childhood. Do childhood adversities have a connection with the development of peptic ulcer in adulthood?

## MATERIALS AND METHODS

The Health and Social Support Study (HeSSup) is a prospective etiological follow-up study of the psychosocial health of the Finnish working-aged population. The HeSSup population is comprised of a stratified random sample drawn from the Finnish Population Register in four age groups: 20-24, 30-34, 40-44 and 50-54. The survey was carried out by postal questionnaire during 1998. Forms were returned by 25 898 individuals; a response rate of 40.0%. A follow-up was sent during 2003 to all those who responded to the first questionnaire. Altogether 19 626 individuals returned the follow-up questionnaire; a response rate of 75.8%. The Turku University Central Hospital Ethics Committee had approved the study.

The sample in 1998 was subjected to a thorough analysis of non-response<sup>[12]</sup>. The analysis was made using the official statistics of the Finnish population for the respective age groups in 1998 to assess whether the study population adequately represented the Finnish population. The major reason for refusal to participate was suspicion as to the purpose behind the request for written consent. Less educated, divorced, widowed and unemployed recipients and those on disability pension were least willing to participate. Differences in physical condition between the study participants and the general population were, however, small.

The participants were asked whether or not a doctor had told them that they have or have had a peptic ulcer. The analyses focused on those who responded affirmatively to both the baseline and the follow-up questionnaire ( $n = 718$ ). Those who did not report a peptic ulcer in either questionnaire ( $n = 17 677$ ) were taken as the control group. It is noteworthy that those administered a new peptic ulcer during the five-year period were not included in the analyses.

The participants were asked to think about their childhood adversities in terms of the following questions, most of them successfully used in a nationwide interview

**Table 1** Kappa coefficients of responses between questionnaires in 1998 and 2003

	$\kappa$ (95% CI)	
	Peptic ulcer	No peptic ulcer
Parents divorced	0.94 (0.91-0.98)	0.90 (0.89-0.91)
Long-lasting financial difficulties in the family	0.72 (0.64-0.79)	0.74 (0.73-0.76)
Serious conflicts in the family	0.71 (0.64-0.78)	0.72 (0.71-0.74)
Often afraid of some member of the family	0.64 (0.55-0.73)	0.71 (0.69-0.72)
Someone in the family seriously or chronically ill	0.55 (0.47-0.63)	0.62 (0.61-0.64)
Someone in the family had problems with alcohol	0.82 (0.76-0.87)	0.84 (0.83-0.85)

survey on living conditions<sup>[13]</sup>: (1) “Did your parents divorce?”; (2) “Did your family have long-lasting financial difficulties?”; (3) “Did serious conflicts arise in your family?”; (4) “Were you often afraid of some member of your family?”; (5) “Was someone in the family seriously or chronically ill?”; (6) “Did someone in the family have problems with alcohol?”. The alternative answers were Yes, No or I do not know. Only the first two options were included in the statistical analyses. The number of childhood adversities per individual was determined. Childhood in the questionnaires, however, was not defined according to age. To confirm the reliability of the answers concerning childhood adversities, the kappa coefficient was used to assess associations between the questionnaires in 1998 and 2003. The coefficient varied between 0.55 and 0.94 among those reporting peptic ulcer and between 0.62 and 0.90 among controls (Table 1).

Participants were asked whether or not they had ever smoked. Smokers were considered those who currently smoked at least five cigarettes daily. Doses and frequency of alcohol use were also asked about and the total amount of alcohol consumed was calculated. Consumption of alcohol drinking was calculated, and at least 175 g alcohol during a week among women and at least 263 g among men was rated as heavy drinking. These limits were set because women achieve higher blood alcohol concentrations than men after drinking equivalent amounts of alcohol.

The Reeder stress inventory<sup>[14]</sup>, a 4-item questionnaire instrument previously widely used, was applied to measure the general sense of stressfulness in daily life. The inventory comprises the following four statements: (1) “In general I am usually tense or nervous”; (2) “There is a great amount of nervous strain connected with my daily activities”; (3) “At the end of the day I am completely exhausted mentally and physically”; and (4) “My daily activities are extremely trying and stressful.” Participants indicate the extent to which each statement applies to them using a 5-point Likert scale (0-4). The mean value was calculated and multiplied by four, the computed value thus indicating the amount of stress. The proportion of those having a stress point higher than the upper quartile ( $\geq 12$ ) was calculated.

**Table 2** Occurrence of childhood adversities among peptic ulcer patients and controls

	Peptic ulcer ( <i>n</i> = 604-673, %)	No peptic ulcer ( <i>n</i> = 15 545-17 188, %)	Difference (%-units)	<i>P</i> value
Long-lasting financial difficulties in the family	45.2	26.8	18.4	< 0.001
Someone in the family seriously or chronically ill	42.3	26.6	15.7	< 0.001
Serious conflicts in the family	32.7	27.2	5.5	0.003
Someone in the family had problems with alcohol	30.2	25.1	5.1	0.003
Often afraid of some member of the family	19.6	13.4	6.2	< 0.001
Parents divorced	18.0	16.0	2.0	0.173

**Table 3** Age distribution and occurrence of risk factors among peptic ulcer patients and controls

	Women			Men		
	Peptic ulcer ( <i>n</i> = 344-362, %)	No peptic ulcer ( <i>n</i> = 10 233-10 975, %)	<i>P</i> value	Peptic ulcer ( <i>n</i> = 326-350, %)	No peptic ulcer ( <i>n</i> = 5970-6667, %)	<i>P</i> value
Age group (yr)						
25-29	8.5	28.7		4.0	22.6	
35-39	19.5	23.4		8.5	23.2	
45-49	25.3	24.3		26.8	25.2	
55-59	46.7	23.6		60.7	29.0	
Smoking						
Current smoking, ≥ 5 cigarettes daily	29.7	16.6	< 0.001	37.7	22.8	< 0.001
Heavy drinking						
> 175 g alcohol/wk	5.0	3.8	0.253			
> 263 g alcohol/wk				10.3	7.7	0.080
Stress						
Reeder points ≥ 12	32.9	20.9	< 0.001	32.8	22.8	< 0.001
Use of nonsteroidal anti-inflammatory drugs						
At least 2 mo during the last year	33.2	16.2	< 0.001	21.9	9.3	< 0.001

Regarding the matter of NSAID use, participants were asked how often they had used them during the last year. The alternative answers were “not at all”, “less than 10 d”, “10-59 d”, “2-6 mo” and “more than 6 mo”. In the analyses at least two months’ consumption during the last year was taken to indicate NSAID use.

The analyses were made using the SAS System for Windows, release 9.1. Statistical significance for the occurrence of adversities was tested with  $\chi^2$ -test. The results were considered significant at  $P < 0.05$ . Age- and sex-adjusted odds ratios (OR) in the logistic regression analysis were calculated (Model 1). The same analyses were carried out with adjustment for both age and sex and smoking (Model 2), for age and sex, smoking and heavy drinking (Model 3), for age and sex, smoking, heavy drinking and stress (Model 4), and also for age and sex, smoking, heavy drinking, stress and current NSAID use (Model 5).

## RESULTS

The most common childhood adversities to emerge were long-lasting financial difficulties in the family, serious conflicts in the family and someone in the family having been seriously or chronically ill (Table 2). All adversities reported were more common among peptic ulcer patients than among controls. Alcohol problems in the family and

fear of some member of the family were also more common among peptic ulcer patients than among controls. With regard to parental divorce, there was no statistically significant difference between the two groups.

Among both genders the life-time prevalence of peptic ulcer increased with age, the tendency being, however, more apparent among men than among women. In the oldest age group the life-time prevalence was over 7% among men and nearly 5% among women. Among men, more than half, and among women, almost half, of the peptic ulcer patients belonged to the oldest age group (Table 3).

Current smoking was more common among peptic ulcer patients than among controls (Table 3). With regard to heavy drinking, there were no differences between ulcer patients and controls. The proportion of subjects scoring Reeder’s stress points more than the upper quartile was greater among patients than among controls, the difference being ten percentage units among both genders. NSAID use was twice as common among patients as among controls.

The total number of childhood adversities per individual was greater among peptic ulcer patients than among controls. At least two adversities had been experienced by 46% of patients *vs* 33% of controls. No adversity had been experienced by 28% of patients *vs* 43% of controls.

Table 4 Childhood adversities in the multivariate logistic analysis for peptic ulcer

	OR (95% CI)				
	Model 1	Model 2	Model 3	Model 4	Model 5
Long-lasting financial difficulties in the family	2.01 (1.71-2.38)	1.90 (1.60-2.26)	1.88 (1.58-2.23)	1.77 (1.48-2.11)	1.73 (1.45-2.07)
Someone in the family seriously or chronically ill	1.67 (1.42-1.96)	1.66 (1.41-1.96)	1.64 (1.39-1.94)	1.59 (1.34-1.88)	1.53 (1.29-1.82)
Serious conflicts in the family	1.47 (1.23-1.75)	1.33 (1.11-1.60)	1.33 (1.11-1.60)	1.24 (1.03-1.50)	1.22 (1.01-1.47)
Someone in the family had problems with alcohol	1.45 (1.22-1.72)	1.37 (1.14-1.63)	1.36 (1.14-1.62)	1.30 (1.09-1.56)	1.27 (1.06-1.52)
Often afraid of some member of the family	1.61 (1.32-1.97)	1.46 (1.18-1.81)	1.44 (1.16-1.78)	1.31 (1.05-1.62)	1.26 (1.01-1.57)
Parents divorced	1.60 (1.30-1.97)	1.40 (1.13-1.74)	1.40 (1.13-1.74)	1.37 (1.10-1.71)	1.37 (1.10-1.71)

Model 1: Age- and sex-adjusted; Model 2: Age- and sex-adjusted and also adjusted for smoking; Model 3: Age- and sex-adjusted and also adjusted for smoking and heavy drinking; Model 4: Age- and sex-adjusted and also adjusted for smoking, heavy drinking and stress; Model 5: Age- and sex-adjusted and also adjusted for smoking, heavy drinking, stress and NSAID use (at least 2 mo during the last year).

Age- and sex-adjusted ORs of childhood adversities for peptic ulcer were statistically significant, indicating that participants with childhood adversities had a higher proportional risk of developing peptic ulcer (Table 4). Adjusting also for smoking, heavy drinking, stress and current NSAID use had no further influence. Long-lasting financial difficulties in the family had the greatest influence.

## DISCUSSION

The principal finding in this study was that individuals reporting peptic ulcer have experienced significantly more childhood adversities than the general population. Life events include not only family problems but also financial problems and those concerning personal security. All of the childhood adversities investigated were statistically significant after adjustment for age. Adjusting for lifestyle issues such as smoking and heavy drinking had a slight influence. It is noteworthy that stress and current NSAID use had no further influence.

Findings in a previous Norwegian study did not support the concept that peptic ulcer is a psychosomatic disorder<sup>[15]</sup>. However, childhood adversities have been found in association with other diseases, for example coronary heart disease<sup>[16]</sup> and migraine<sup>[17]</sup>, and also with disability pensions<sup>[18]</sup>. According to our findings, childhood adversities are also associated with self-reported peptic ulcer. Self-reported childhood trauma has been found to be associated with an increased risk of a range of physical illnesses during adulthood, including peptic ulcer<sup>[19]</sup>. In a Danish study poor socio-economic status emerged as an important risk factor for peptic ulcer disease which exerts its effect independently of *H. pylori* infection<sup>[20]</sup>. In functional dyspepsia the role of psychosocial factors continues to be the subject of debate<sup>[21]</sup>. In this respect our findings support those previous studies.

The study material may be considered representative of the Finnish working-aged population, although the response rate in 1998 was only 40%. Careful non-response analysis indicated that respondents and non-respondents were comparable with respect to the most important demographic variables<sup>[12]</sup>. Moreover, the rate of response to the follow-up questionnaire was high.

As it is a question of self-reported peptic ulcer, we

cannot be completely sure whether the subjects really have a pathological condition meeting the diagnostic criteria. Some of the subjects reporting peptic ulcer may only have non-ulcer dyspepsia. However, we regarded as peptic ulcer patients only those reporting the disease in two questionnaires carried out at 5-year intervals.

There was no way of knowing whether the ulcer reported was a duodenal or a stomach ulcer. We did not enquire whether or not the respondents had undergone gastroscopies, and have no data on the possible occurrence of complications. In Finland most uncomplicated peptic ulcers are treated in primary health care. Neither did we ask whether or not the participants had received antibiotic therapy for *H. pylori* infection.

It is possible that ulcer patients reported childhood adversities more readily than did controls. Perhaps individuals with psychological stress or distress also tend to report on a peptic ulcer more easily than other people. Although retrospective studies of adverse childhood experiences have a worthwhile place in research<sup>[22]</sup>, we must concede that there are unanswered questions with regard to selective recall, and this may be considered a weakness of our study. The reports of childhood adversities are subjective, based upon memories where the time span from childhood to adulthood is not further defined. This notwithstanding, the kappa coefficients confirming the reliability of the answers may be considered quite high and also alike for the ulcer and non-ulcer groups, indicating that peptic ulcer patients had not remembered childhood adversities more readily than controls.

With regard to lifestyle issues and NSAID use there are some unknown concerns. Although we could calculate the total amount of alcohol consumed, we do not know the amount of cigarettes the respondents had smoked. Neither do we know the daily doses of NSAID use. We therefore considered it reasonable to dichotomize these variables. This may be a confounding factor. In our opinion, however, it hardly had an impact on our findings.

Peptic ulcer has been considered a valuable model for understanding the complex interactions among psychosocial, socioeconomic and infectious factors in causing organic disease<sup>[23]</sup>. Childhood adversities may be associated with lower socioeconomic level and modest living conditions, which may in part increase the risk



of infection by *H pylori*<sup>[24]</sup>. Moreover, children living in the most crowded conditions are at the greatest risk for *H pylori* acquisition<sup>[25]</sup>. Unfortunately our data did not contain details about the respondents' socioeconomic status and housing conditions.

What then are the reasons for the associations between childhood adversities and self-reported peptic ulcer? In this respect childhood adversities may predispose to *H pylori* infection. It is also possible that childhood adversities may predispose to a variety of aches and pains which are alleviated by NSAIDs. We must also admit that we do not know the possible role of genetic factors concerning e.g. the vulnerability of the gastric mucosa. Moreover, vigilant concern and anxiety might affect chronic automatized coping mechanisms and thus stress responses later in life.

Although the occurrence of peptic ulcer has declined due to widespread empirical treatment of dyspepsia, the peptic ulcer patient is still a common client in doctors' offices. Only a few decades ago peptic ulcer was considered almost exclusively a psychosomatic disease. When the association with *H pylori* was discovered in the 1980s the disease was regarded mainly as an infection, and the stress theory fell into oblivion. According to our findings there is reason to believe that stress factors during childhood still have a connection with the development of peptic ulcers. We thus venture to state that there are also social factors in the background. Childhood adversities are not necessarily true risk factors for peptic ulcer, but may play a predictive role in the development of the disease. A more comprehensive understanding of peptic ulcer patients is worth aspiring to.

## COMMENTS

### Background

*Helicobacter pylori* (*H pylori*), nonsteroidal anti-inflammatory drugs (NSAID) and smoking are the most important risk factors for peptic ulcer. However, between 5% and 20% of patients with gastric or duodenal ulcers lack an identifiable organic etiology. Psychological stress may have an impact on the onset and course of ulcer disease. Very little is known as to whether childhood adversities involving financial problems, conflicts in the family, problems with alcohol, and matters of personal security are associated with peptic ulcer.

### Research frontiers

Childhood is an important and vulnerable period in individual development. The research hotspot is whether there has been something particular in the social circumstances of peptic ulcer patients during childhood. Do childhood adversities have a connection with the development of peptic ulcer in adulthood?

### Innovations and breakthroughs

The most common childhood adversities to emerge were long-lasting financial difficulties in the family, serious conflicts in the family and someone in the family having been seriously or chronically ill. Alcohol problems in the family and fear of some member of the family were also more common among peptic ulcer patients than among controls. All of the childhood adversities investigated were statistically significant after adjustment for age. Adjusting for life style issues such as smoking and heavy drinking had only a slight influence.

### Applications

The study results suggest that stress factors during childhood have a connection with the development of peptic ulcers. Childhood adversities may play a predictive role in the development of the disease. A more comprehensive understanding of peptic ulcer patients is worth aspiring to.

### Terminology

Peptic ulcer: An ulcer on the mucous membrane of stomach (gastric ulcer) or

duodenum (duodenal ulcer) that is usually acidic and thus extremely painful. Childhood adversities: Negative life experiences during childhood such as long-lasting financial difficulties, serious conflicts in the family, fear of some family member, someone in the family being seriously or chronically ill, and someone in the family having had problems with alcohol.

### Peer review

This work is well conducted. The results from this work shows that there is a reason to believe that *H pylori* is not the only etiological factor regarding peptic ulcer but others factors like childhood adversities may play a predictive role in the development of peptic ulcer. According to this survey, it is reasonable to believe that stress factors during childhood maintain a connection with the development of peptic ulcers.

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