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EPIDEMILOGICAL CHARACTERISTICS AND ASSOCIATED FACTORS OF *HELICOBACTER PYLORI* INFECTION AMONG CHILDREN AND HOUSEHOLD MEMBERS OF TAY AND MUONG ETHNIC COMMUNITIES

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The thesis can be found:

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INTRODUCTION

The International Cancer Research Organization has classified *Helicobacter Pylori (HP)* in the risk group I causing stomach cancer. However, the mechanism of *HP* causing cancer has not been fully understood. Beside of causing stomach cancer, *HP* is also a major cause of chronic gastritis in adults and children. It is the main cause of gastro-duodenal ulcer leading to serious health consequences as well as affects to quality of life. Although information on *HP*'s biological characteristics, physiological and pathogenic roles has been studied in many years, the updated knowledge regularly provides the basis for new diagnostic methods and strategies, effective treatment but pathological situations and the consequences of *HP* infection are still a global challenge.

Serological studies worldwide have shown that the prevalence of *HP* varies among ethnic groups in countries. In Vietnam, research on *HP* infection has been conducted scatteredly since the early 2000s. These studies have not been fully implemented in ethnic groups in Vietnam, and mostly on adults. Available data are collected from Kinh, Thai, Khmer, Ede, Nung and H'mong ethnic communities but no studies was conducted among the Tay and Muong communities. In developing countries, children infected with *HP* very early, there are cases of newborn patients. Human leukocyte antigen (HLA) is the system that determines the host's response to the infection microbiological factors. HLA polymorphism plays an important role for changing individual immune responses to different antigens, contributing to certain susceptibility or disease resistance. The relationship between HLA alleles classes, especially HLA-DQ with bacterial susceptibility as well as *HP* treatment efficacy, has been found in studies worldwide. In Vietnam, there has been no research on this relationship. We conducted this research to determine the prevalence, and associated factors of *HP* infection in the two ethnic groups with a large proportion of the population after the Kinh group, including Tay and Muong ethnic groups focusing on children and household members. The research results will contribute to providing information to develop epidemiological maps of *HP* infection situation in Vietnam. In addition, this result will be a scientific evidence to help policy makers have strategies to protect the health of ethnic minorities, an issue that the Vietnam Communist Party and the Government are concerning to ensure social equity in health care.

Research objectives

1. Describe some epidemiological characteristics of *Helicobacter Pylori* infection in children from 6 months to 18 years, and household members of Tay and Muong ethnic groups in Lang Son and Hoa Binh provinces in 2013-2014,

2. Determine factors related to *Helicobacter Pylori* infection in research groups,

3. Describe the distribution of genotypes of human DQB1 leukocyte antigen (HLA-DQB1) related to *Helicobacter Pylori* infection in children aged from 6 months to 18 years old.

Findings of this research

There have not many studies on the situation of *HP* infection in children and in the Tay and Muong ethnic groups.

Identification of epidemiological characteristics of *HP* infection in Tay and Muong people in Lang Son, Hoa Binh and associated factors of *HP* infection such as age group and *HP* infection status of

household members, hygiene behavior in eating, environmental sanitation, economic status, large family sharing a house, and education of mothers.

This is the first research described the distribution of HLA-DQB1 genotypes using molecular biology techniques, identifying a link to *HP* infection in children in Vietnam.

STRUCTURE OF THE THESIS

This thesis includes 112 pages, exept references and appendixes; having 29 tables, 1 map, and 1 figure. The thesis consists of Introduction: 2 pages; Background: 40 pages; Method: 22 pages; Results: 28; Discussion: 35 pages; Conclusion: 2 pages, and Recommendation: 1 page.

Chapter 1: BACKGROUND

1.1. Research on *Helicobacter Pylori*

Helicobacter Pylori was found in 1875 and was originally named *Campylobacter pylorid*. However, it was renamed to *Helicobacter* in 1989 to reflect morphological characteristics: stick-shaped and twisted in vivo.

In 1983, Warren and Marshall determined the link between *HP* spirochetes and stomach disease. Subsequently, the American National Institutes of Health announced that *HP* can be the cause of gastro-duodenal ulcers and recommend antibiotics for treatment.

1.2. Morphological characteristics, pathogenicity of *Helicobacter Pylori*

In humans, there are only two *Helicobacter* strains, *HP* and *H. heilmannii* can reside in human stomach and l cause gastro-duodenal disease.

In terms of morphology, *HP is a helix-shaped (classified as a curved* or S-shaped *rod*), Gram-negative, 1.5-5 µm long with diameter of 0.3-1 µm and a tuft of 5 to 7 polar sheathed flagella. *HP*'s shape pattern only met when fresh screening or staining of histopathology of biopsy samples. In culture medium, *HP* has a longer morphology and lower twist. Based on morphological characteristics, *HP* can be detected based on Gram staining or divergence microscopic examination.

Helicobacter Pylori is a bacterium that lives in human gastric environment with very high levels of HCl acid (pH <2). *HP* has characteristics that are adaptive to living conditions: *HP*'s urease enzyme system is used to convert urea into two alkaline substances, including Ammonia and Bicarbonate, creating an alkaline cloud around it. Torsion cell structure and high-energy whip set allow *HP* to be able to move quickly and escape the environment of high acidity. This bacterium is present only in the duodenum if there is a type of gastric hyperplasia there, and clings to the islets of the stomach cell in the duodenum. *HP* has the ability to attach to the target tissue to cause disease because of the tissue-specific adhesives, such as N-acetyl-neureminyl-lactose, which helps *HP* cling to red blood cells.

HP infection in the stomach causes a strong immune response of the host body. Immunological factors of bacteria have not been clarified. Currently, only certain *HP* antigenic components are identified, such as CagA. Thanks to a rich enzyme system like catalase, superoxyd dismutase and urease to destroy macrophage pathways of macrophages. In addition, the host's immune responses simultaneously damage the gastric mucosa.

1.3. Epidemiology of *Helicobacter Pylori* infection worldwide and in Vietnam

The prevalence of *HP* in developing countries is much higher than in developed countries. Children are infected very early, the infection prevalence in 5-year-old children is 5% and can

increase to 70-90% in adults. However, the prevalence is different between countries. In general, the incidence in children is in the range of 1-5% per year, but it can be more than 20% per year for developing countries with a high prevalance of infections. Reinfection after *HP* eradication treatment is low in developed countries, and high in developing countries. This proportion is up to 25% in Vietnam, meaning that up to 1/4 of the children successfully treated will be re-infected. In developed countries, this proportion is only about 1%/person/year, and the self-recovered rate is similar (1.8% in children and 1.5% in adults) but the cumulative incidence is increasing. It demonstrates that reinfection rates often change.

Vietnam is located in the region with quite high prevalence of *HP* infection, and it varies in different areas. *HP* infection prevalence in the research of Nguyen Van Bang et al. (2004) among 824 children aged 6 months to 15 years old without symptoms of gastrointestinal disease, treated in the Department of Pediatrics, Bach Mai Hospital, was 34%. The research results of Hoang Thi Thu Ha (2005) in children 6-18 years old showed an infection prevalence of 37.6%.

1.4. Transmission mechanism and related factors

1.4.1. Human to human transmission

Gastrointestinal transmission is very common, especially in the childhood period. In addition, poor hygiene practices in eating, breast feeding, and vomit act as a means of transporting infectious bacteria.

Oral-oral transmission may be due to *HP* infection in dental plaque and to the saliva of *HP* infected patients. In the condition of poor hygiene, *HP* can infect by fecal-oral route.

Transmission from mother to child through breast milk is due to the presence of *HP* bacteria in the milk that can be caused by bacterial infection from the nipple or finger.

1.4.2. External body reservoir and the role of environmental factors in *Helicobacter Pylori* transmission

Food can be contaminated from water containing *HP* during preparation and cleaning procces, especially in poor sanitary conditions.

HP can exist in milk for a short time. In addition, there is evidence of a link between food and risk of *HP* infection, for example, people who eat raw vegetables are more likely to be infected with *HP*.

With the assumption that *HP* is in the feces, flies can play a role in transporting *HP* from feces to food. This hypothesis is consistent with the situation of *HP* infection in the world. Researchs showed that there is a very high prevalence of *HP* infection in developing countries, where unhygienic latrines are common, while low prevalence was found in developed countries where there are little unhygienic latrines.

1.5. Risk factors for *Helicobacter Pylori* infection

1.5.1. Biological factor

Age is one of the most important factors determining the level of *HP* infection in most epidemiological studies. Children are considered to be vulnerable to *HP* infection. However, the highest prevalence of *HP* infection was found among 2-6-year children, depending on research locations, and different studies.

Gender is found a factor related to the risk of *HP* infection.

The role of blood type with the risk of *HP* infection is still controversial. Many researchers have focused on analyzing the association between ABO blood antigens and *HP* infection. Some researchers have found an association between blood type O and the increase of *HP* infection.

1.5.2. Socio-economic factors

Prevalence of *HP* infection in developed countries are lower than in developing or underdeveloped countries. Previous studies showed that family income is associated with the risk of *HP* infection according to the trend of lower family income, the higher the risk of *HP* infection. It can be argued that in poor and low-income countries, living conditions, sanitation, and behavioral conditions have direct impact on the communities, while, in the developed countries those factors do not affect much on its counterparts.

In addition, education and occupational factors are also associated with the risk of *HP* infection, the lower the educational level, the higher the risk of *HP* infection.

1.5.3. Living condition

The mode of transmission associated with over crowded living conditions can be considered through factors such as household size, number of people per family, housing size, and bed sharing in childhood...

1.6. Desease caused by *Helicobacter Pylori*

Warren and Marshall have identified that *HP* is associated with chronic gastritis. *HP* resides mainly in the gastric region and the stomach's position increases the penetration of mononuclear and mononuclear leukocytes, leading to inflammation and ulceration.

HP infection is a major cause of stomach ulcers in adults. *HP* infection leads to inflammation of the stomach mocosa. If not be treated, this process will become more severe.

HP has been shown to be related to stomach cancer and gastric mucosa lymphoma, however, this mechanism is not well documented.

Recurrent abdominal pain is defined as at least three episodes of pain that occur over at least three months and affect the one's ability to perform normal activities. The role of *HP* as a cause of recurrent abdominal pain is still controversial.

Although there have been many studies in this topic, however, the relationship between *HP* infection and the desease of gastroesophageal reflux in children is still unclear. Among *HP* infection patients, beside of symptoms in the gastrointestinal tract, there are also symptoms out of gastrointestinal track such as anemia, thrombocytopenia, and malnutrition.

1.7. The relationship between leukocyte antigen and *HP* infection

Human Leucocyte Antigen (HLA) may play a special role in the host's immune response to bacterial antigens. Recent studies often focus on assessing the role of HLA class II in relation to the risk of *HP* infection. Class II genotypes are often studied mainly as HLA-DRB1, HLA-DQB1, HLA-DQA1.

Chapter 2. METHODOLOGY

2.1. Site of the research

The research was carried out in Chien Thang, Hoan Trung, Huong Coc, Vu Son communes of Bac Son District, Lang Son province and Ky Son town, Dan Ha commune of Ky Son District, Hoa Binh province.

2.2. Time of the research

The process of sample collection and survey were carried from February 2013 to October 2014.

2.3. Research subjects

Children aged from 6 months to under 18 years and household members of Tay ethnic community in Lang Son province and Muong ethnic community in Hoa Binh province. Those participants were confirmed by the identity cards, household registration books, the fact of sharing the house, and the confirmation of the local authorities.

2.4. Methodology

2.4.1. Research design

- **Cross-sectional survey** (statistical analysis, evaluation of epidemiological characteristics) based on dependent variable is *HP* infection, and independent variables including age, gender, occupation, etc.
- Thiết kế nghiên cứu: mô tả cắt ngang (đánh giá đặc điểm dịch tễ học) dựa vào biến phụ thuộc là tình trạng nhiễm *HP* (ELISA dương tính hoặc âm tính)
- Research tools: interview questionnaire, blood and serology test kits and, and PCR technique.

2.4.2. Sample size

The sample size formula to estimate a prevalence was applied in this research:

$$n = z^2_{1-\alpha/s} \frac{1-P}{\varepsilon^2 P}$$

p: estimated *HP* infection prevalence of the research subjects

ε: permissible relative error between the rate obtained from the sample and the proportion of the population

The calculation with the above formula showed the number of children should be involved the research is 714, for the prevention of refuse or the potential cannot be reached, the number of 800 children was decided. Number of household members (parents, grandparents, brothers, sisters) would be collected as many as they are in each family. In fact, 805 children and 1207 adults were involved in the research.

2.4.3. Sample collection

Lists of households with children from 6 months to 18 years in the study sites in both ethnic groups were made. According to the household lists, the first household was selected, followed by "door to door" household approach until the sample of children is reached at each location. The number of adults participated in the study is dependent on the actual situation.

2.4.4. Data process

Data were entered and analyzed by SPSS 16.0 and other software. The assessment of *HP* infection is calculated separately for each factor by a single regression algorithm with 5% statistical significance.

2.4.3. ELISA technique for determination of *HP* infection status

All households' members with children from 6 months to under 18 years were collected blood samples for blood group classification, diagnosis of *HP* infection by ELISA technique, and identify the risk factors of *HP* infection. The test was performed at the Laboratory of Special Bacteria, Microbiology Department, National Institute of Hygiene and Epidemiology.

2.2.3. Determination of HLA-DQB1 genotype by PCR technique

Polymerase Chain Reaction (PCR) was applied to identify the genotype. The product was dyed with Redsafe and identified under UV light. HLA fusion software was used to get HLA DQB1*xxyy results.

2.5. Ethics

The research was approved by the Medical and Scientific Council of Hanoi Medical University. In addition, the study was also approved by the Department of Health in Lang Son and Hoa Binh provinces. Research subjects are ensured safety in the process of blood sampling, ensuring confidentiality of personal information. The collected data are honest and accurate. The study participants with *HP* positive were reported to the district health center for further examination, endoscopy and treatment appointment.

Chapter 3. RESULTS

3.1. General characteristics of research subjects

Table 3.1. Distribution of subjects according to age and sex

Ethnic group	No. of House hold	No. of subjects	Adults n (%)	Children n (%)	Male n (%)	Female n (%)
Tay	131	1094	618(56.5)	476(43.5)	481(44)	613(56)
Muong	219	918	589(64.16)	329(35.84)	398(43.3)	520(56.7)
Total	350	2012	1207(60)	805(40)	879(43.7)	1133(56.3)

In total, 2012 participants of 131 household of Tay community and 219 household of Muong community were surveyed. Number of adults is 1207, accounts for 60%; number of children is 805, account for 40% of participants.

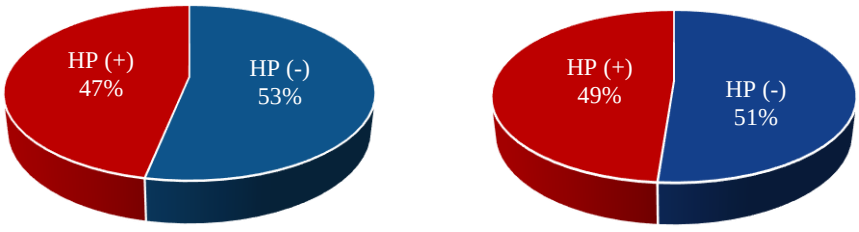
Table 3.2. Distribution of subjects according to age groups

Age group	Tay		Muong	
	No. of Subjects	Proportion (%)	No. of Subjects	Proportion (%)
<3	55	5.0	52	5.7
3-<6	83	7.6	54	5.9
6-<10	153	14.0	82	8.9
10-<15	121	11.1	80	8.7
15-<18	64	5.9	61	6.6
18-<30	120	11.0	117	1.7
30-<40	229	20.9	201	21.9
40-<50	101	9.2	118	12.9
50-<60	100	9.1	83	9.0
≥60	68	6.2	70	7.6

Research subjects are divided into two groups; children (under 18 years) and adults (from 18 years). Each group, then, is divided into five age subgroups. The number of research subjects in each subgroup is quite similar in both two ethnic groups. The number of children of the subgroup of 6 – 10 years is the highest (8,9% in Muong and 14% in Tay ethnic group). The highest subgroup among adults is the subgroup of 30-<40 years with the proportion of 20,9% of Tay and 21,9% of Muong group.

3.2. Prevalence of *Helicobacter Pylori* infection among the studied participants

3.2.1. Prevalence of Helicobacter Pylori infection among the studied participants



Tay (n=1094) Muong (n=918)

Figure 3.1. Prevalence of *Helicobacter Pylori* infection among the studied participants

The proportion of HP infection among the Tay group is 46,8%; the prevalence of HP infection among the Muong group is 48,6%. The difference of two prevalence is not statistically significant.

Table 3.3. Prevalence of *Helicobacter Pylori* infection among studied groups

Group	Tay			Muong			p(1)
	N	*HP*(+) n(%)	OR(95%CI)	N	*HP*(+) n(%)	OR(95%CI)	
Children	476	197(41.4)	1	329	141(42.9)	1	0.678
Adults	618	304(49.2)	1.37(1.08-1.75)	589	307(51.2)	1.45(1.11-1.91)	0.309

p(1): *between Tay and Muong groups*

For Tay people, the prevalence of HP infection among children was 41.4%, and among adults was 49.2%. This prevalence among the Muong was 42.9%, and 52.1%, respectively. The prevalence of HP of children is significantly lower than adults. There is no difference of PH(+) prevalence between two ethnic groups.

3.1.2. HP infection prevalence among children and family members by age group and sex

Table 3.4. Prevalence of *Helicobacter Pylori* infection by age

Sex		Tay			Muong			P(1)
		N	*HP*(+) n(%)	OR(95%CI)	N	*HP*(+) n(%)	OR(95%CI)	
Adults	Male	244	127(52.0)	1.1(0.88-1.21)	246	121(49.2)	0.81(0.58-1.13)	0.526
	Female	374	188(50.3)	1	343	186(54.2)	1	0.289
Children	Male	237	104(43.9)	1.2(0.91-1.39)	152	70(46.1)	1.27(0.82 -1.97)	0.674
	Female	239	93 (38.9)	1	177	71(40.1)	1	0.804
Total	Male	481	251(48.0)	1.04(0.92-1.19)	398	191(48.0)	0.94(0.72-1.23)	0.992
	Female	613	281(45.8)	1	520	257(49.4)	1	0.229

p(1): *between Tay and Muong groups*

The prevalence of HP positive for men and women in Tay community was 48%, and 45.8% respectively. The prevalence among men and women in the Muong ethnic group was 48%, and 49.4%, respectively. There was no statistically significant difference between the prevalence in both sexes.

Table 3.5. Prevalence of *Helicobacter Pylori* in children by age

Age group	Tay			Muong			P(1)
	N	*HP*(+) n(%)	OR(95%CI)	N	*HP*(+) n(%)	OR(95%CI)	
0.5-<3	55	17(30.9)	1	52	17(32.7)	1	0.843
3-<6	83	31(37.3)	1.33(0.64-2.75)	54	22(40.7)	1.45(0.64-3.13)	0.69
6-<10	153	65(42.5)	1.65(0.85-3.18)	82	38(46.3)	1.77(0.81-3.48)	0.57
10-<15	121	50(41.3)	1.57(0.8-3.09)	80	36(45.0)	1.68(0.81-3.48)	0.606
15-<18	64	34(53.1)	1.59(1.09-2.32)	61	28(45.9)	1.74(0.81-3.76)	0.419

p(1): *between Tay and Muong groups*

The prevalence of HP(+) of Tay children is significant increased by age group: the highest prevalence is of the group of 15-<18 years (53,1%), the lowest prevalence is the group of 6 months to under 3 years (30,9%), this difference is statistically significant with OR=1,59 (95%CI:1,09-2,32). In Muong group, the prevalence of HP (+) is also lowest in the children group of 6 months to under 3 years

(30,9%) but the age group having the highest prevalence is 6-<10 years (46,3%). There is no statistically significant difference of the HP (+) prevalence between equal age groups of the two ethnic communities.

Table 3.7. Trend of *Helicobacter Pylori* by aged groups in the two communities

Age group	Tay			Muong		
	N	*HP*(+)n(%)	ptrend	N	*HP*(+)n(%)	ptrend
0.5-<3	55	17(30.9)	0.000225	52	17(32.7)	0.001543
3-<6	83	31(37.3)		54	22(40.7)	
6-<10	153	65(42.5)		82	38(46.3)	
10-<15	121	50(41.3)		80	36(45.0)	
15-<18	64	34(53.1)		61	28(45.9)	
18-<30	120	65(54.2)		117	59(50.4)	
30-<40	229	107(46.7)		201	101(50.2)	
40-<50	101	45(44.5)		118	61(51.7)	
50-<60	100	64(64.0)		83	48(57.8)	
≥60	68	33(48.5)		70	38(54.3)	

ptrend: trend analysis of HP infection by age groups

Trend analysis combining both adult and child groups was performed by a trend test. In the Tay ethnic group, HP infection prevalence tends to increase significantly by age group (ptrend = 0.000225). This trend is also found in the Muong ethnic group with p = 0.001543.

3.2.3. The association between Helicobacter Pylori infection and family members, having disease history and antibiotic use

Table 3.8. The association between *Helicobacter Pylori* infection in children and infection *Helicobacter Pylori* of family members

HP infection status		Tay			Muong		
		N	*HP*(+)n(%)	OR(95%CI)[(2)]	N	*HP*(+)n(%)	OR(95%CI)[(2)]
Mother	(-)	154	45(29.2)	1	144	61(42.4)	1
	(+)	124	78(62.9)	4.04(2.42-6.75)	141	66(46.8)	1.19(0.74-1.92)
Father	(-)	123	42(34.1)	1	121	52(43.0)	1
	(+)	91	42(46.15)	1.68(0.95-2.9)	121	57(47.1)	1.13(0.67-1.90)
Father/Mother	(-/-)	71	22(30.9)	1	56	28(50.0)	1
	(+/-)	58	21(36.2)	1.12(0.52-2.41)	104	42(40.4)	0.68(0.35-1.31)
	(+/+)	40	23(57.5)	1.68(1.1-2.5)	65	36(55.0)	1.04(0.71-1.51)
Siblings	(-)	85	22(25.9)	1	122	44(36.1)	1
	(+)	63	39(61.9)	4.64(2.26-9.52)	91	45(49.5)	1.7(1.09-2.01)

Grandfather	(-)	15	6(40.0)	1	30	16(53.3)	1
	(+)	27	22(75.8)	11.1(1.71-72.3)	34	19(55.9)	1.05(0.38-2.95)
Grandmother	(-)	57	13(22.8)	1	65	33(50.8)	1
	(+)	29	22(75.8)	11.6(3.82-35.1)	31	19(61.3)	0.63(0.26-1.52)

OR(95%CI)[(2)]: *Adjusted for age and sex*

Among Tay people, children have relatives (mother, parents, grandparents, siblings) with HP infection have higher prevalence of HP infection than children without HP infected relatives; children whose mothers were infected with HP were 4.04 times more likely to be infected than those with HP uninfected mothers (95%CI: 2.42-6.75); children having siblings HP positive were at risk of being 4.64 times higher (95% CI: 2.26-9.52) compared with those do not have; children with grandparents with HP(+) are at 11.1 and 11.6 times higher risk of infection than children with grandfather (95%CI: 1.71-72.3), and grandmother (95%CI: 3,82-35.1). For the Muong, children with parents, grandparents infected with HP also have higher prevalence of HP infection than children living in families with parents, grandparents who are not infected; however, this difference was not statistically significant; children with siblings HP(+) have 1,7 time higher risk of HP infection than the rests (95%CI:1,09-2,01).

Table 3.9. The association between *Helicobacter Pylori* infection in children and having health conditions

Health conditions		Tay			Muong		
		N	***HP*(+)n(%)**	**OR(95%CI)[(2)]**	**N**	***HP*(+)n(%)**	**OR(95%CI)[(2)]**
Having history of gastrointestinal diseases	(-)	218	86(39.4)	1	413	170(41.2)	1
	(+)	62	31(50.0)	1.53(0.87-2.7)	31	13(41.9)	1.03(0.49-2.16)
Having gastrointestinal diseases	(-)	255	89(34.9)	1	424	172(40.6)	1
	(+)	54	29(53.7)	1.77(0.97-3.22)	43	20(46.5)	1.27(0.67-2.39)
Having history of allergy	(-)	223	89(39.9)	1	387	159(41.1)	1
	(+)	73	34(46.6)	1.31(0.77-2.23)	64	27(42.2)	1.04(0.61-1.78)

OR(95%CI)[(2)]: *Adjusted for age and sex*

In both groups, children having history of gastrointestinal diseases, gastrointestinal diseases, and history of allergy had higher prevalence of HP infection compared to children without those diseases. However, this difference was not statistically significant.

Table 3.10. The association between *Helicobacter Pylori* infection in adults and HP infection of spouses

Spouses	Tay			Muong		
	N	***HP*(+)n(%)**	**OR(95%CI)[(2)]**	**N**	***HP*(+)n(%)**	**OR(95%CI)[(2)]**
HP(-)	132	61(46.2)	1	134	57(42.2)	1
HP(+)	138	80(58.0)	1.6(0.99-2.57)	162	99(61.1)	2.12(1.3-3.38)

OR(95%CI)[(2)]: *Adjusted for age and sex*

There was an association between HP infection, and the HP infection status of their spouses. People having wife or husband with HP infection had higher prevalence of HP infection compared with those without this disease (58% compared to 46.2% among Tay people, and 61.1% in comparison with 42.2% among Muong people). However, significant difference was only found in Muong group, OR= 2.12 (95%CI:1.3-3.38).

Table 3.11. The association between *Helicobacter Pylori* infection in adults and having health conditions

Health conditions		Tay			Muong		
		N	*HP*(+)n(%)	OR(95%CI)[(2)]	N	*HP*(+)n(%)	OR(95%CI)[(2)]
Having history of gastrointestinal diseases	(-)	341	183(53.7)	1	246	137(55.7)	1
	(+)	177	88(49.7)	0.92(0.77-1.1)	252	125(49.6)	0.89(0.75-1.05)
Having gastrointestinal diseases	(-)	388	197(50.8)	1	298	163(54.7)	1
	(+)	185	97(52.4)	1.03(0.87-1.22)	196	95(48.5)	0.88(0.74-1.04)
Having history of allergy	(-)	440	233(53.0)	1	361	198(54.8)	1
	(+)	100	52(52.0)	0.98(0.79-1.2)	144	68(47.2)	0.86(0.7-1.04)

OR(95%CI)[(2)]: *Adjusted for age and sex*

No significant difference was found between people with health conditions of having history of gastrointestinal diseases, having gastrointestinal diseases, having history of allergy in both groups.

Table 3.12. The association between *Helicobacter Pylori* infection in children with history of antibiotic use

Antibiotic use		Tay			Muong		
		N	*HP*(+)n(%)	OR(95%CI)[(2)]	N	*HP*(+)n(%)	OR(95%CI)[(2)]
Within less than 1 month	No	315	137(43.5)	1	179	77(43)	1
	Yes	142	50(35.2)	0.74(0.46-1.65)	127	47(37)	0.82(0.54-1.87)
Within last 12 months	No	188	85(45.2)	1	73	33(45.2)	1
	Yes	249	96(38.6)	0.86(0.55-1.2)	238	104(43.7)	0.95(0.44-1.42)

OR(95%CI)[(2)]: *Adjusted for age and sex*

Children used antibiotic in last month or last 12 months had lower prevalence of HP infection in comparison with children did not use, the difference was not statistically significant.

Table 3.13. The association between *Helicobacter Pylori* in the adults and history of antibiotic use

Antibiotic use		Tay			Muong		
		N	*HP*(+)n(%)	OR(95%CI)[(2)]	N	*HP*(+)n(%)	OR(95%CI)[(2)]
Within less than 1 month	No	365	195(53.4)	1	338	168(49.7)	1
	Yes	191	92(48.2)	0.91(0.73-1.22)	201	99(49.3)	0.98(0.62-1.2)
Within last 12 months	No	245	142(58.0)	1	182	95(52.2)	1
	Yes	238	142(59.6)	0.73(0.51-1.03)	307	157(51.1)	0.95(0.66-1.38)

OR(95%CI)[(2)]: *Adjusted for age and sex*

The study did not find any association between HP infection among the adults and history of antibiotic use in both groups.

3.2.4. The association between Helicobacter Pylori infection and eating habits, and hygiene

Table 3.14. The association between *Helicobacter Pylori* infection in children and eating habits, and hygiene

Habits		Tay			Muong		
		N	*HP*(+) n(%)	OR(95%CI)[(2)]	N	*HP*(+) n(%)	OR(95%CI)[(2)]
Using hand to collect food	No	218	85(39)	1	122	18(14.8)	1
	Sometime	169	72(42.6)	1.1(0.85-1.4)	153	103(67.3)	4.56(2.9-7.0)
	Usually	76	34(44.7)	1.14(0.85-1.55)	42	13(31.0)	2.09(1.12-3.9)
Sharing food	No	240	109(45.4)	1	193	80(41.5)	1
	Yes	218	82(37.6)	0.82(0.66-1.03)	131	57(43.5)	1.03(0.79-1.34)
Washing hand before eating	Often	27	15(55.6)	1	51	18(35.3)	1
	Usually	260	103(39.6)	0.52(0.23-1.16)	92	14(15.2)	0.43(0.23-0.79)
	Sometime	83	34(41.0)	0.55(0.23-1.33)	39	13(33.3)	0.94(0.52-1.68)
	No	38	16(42.1)	0.75(0.45-1.25)	97	79(81.4)	2.3(1.57-3.38)
Washing hand after using toilet	Yes	145	50(34.5)	1	120	52(43.3)	1
	No	323	140(43.3)	1.25(0.97-1.62)	195	82(42.1)	1.03(0.79-1.3)
Hygiene habits after going to the toilet	Clean by tissue	369	155(42.0)	1	138	55(39.9)	1
	Clean by water	58	21(36.2)	0.86(0.60-1.23)	115	47(40.9)	1.02(0.76-1.38)
	Both	40	16(40.0)	0.64(0.64-1.41)	44	18(40.9)	1.0(0.65-1.51)

Breast feeding	≥12 months	366	138(37.7)	1	208	91(43.8)	1
	<12 months	76	32(42.1)	1.2(0.72-2.01)	120	50(41.7)	0.89(0.56-1.42)
Chewing and feeding	No	170	63(37.0)	1	214	80(37.4)	1
	Yes	272	115(42.3)	1.3(0.72-1.65)	114	61(53.5)	2.0(1.76-2.32)

OR(95%CI)[(2)] *Adjusted for age and sex*

The study did not find any association between HP infection in the Tay children and habits such as using hand to collect foods, sharing foods, washing and before eating, duration of breast feeding (p>0.05). For the Muong children, there were associations between HP infection, and chewing and feeding (children were feed by chewing foods had 2 times higher than those without this habit, (95%CI:1.76-2.32; prevalence of 53.5% compared to 37.4%)); using hand to collect food (children who often and sometime use their hand to collect food had the risk of 2.09, and 4.56 times having HP infection compared to those did not (95%CI:1.12-3.9 and 95%CI:2.9-7); Did not wash their hand before eating was a risk factor, OR=2.3 (95%CI:1.57-3.38).

Table 3.15. The association between *Helicobacter Pylori* infection in adults and eating habits, and hygiene

Habits		**Tay**			**Muong**		
		N	***HP*(+) n(%)**	**OR(95%CI)[(2)]**	**N**	***HP*(+) n(%)**	**OR(95%CI)[(2)]**
Using hand to collect food	No	327	169(51.7)	1	369	190(51.5)	1
	Yes	234	122(52.1)	1.05(0.86-1.19)	191	95(49.7)	0.97(0.68-1.45)
Sharing food	No	247	130(52.6)	1	332	166(50.0)	1
	Yes	297	159(53.5)	1.01(0.86-1.29)	243	129(53.1)	1.13(0.71-1.33)
Washing hand before eating	Often	32	11(34.4)	1	127	65(51.2)	1
	Usually	366	197(53.8)	1.56(1.04-4.74)	118	79(43.6)	0.85(0.67-1.08)
	Sometime	109	51(46.8)	1.36(0.81-2.28)	56	15(26.8)	0.52(0.32-0.83)
	No	28	17(60.7)	1.76(1.0-3.1)	130	111(85.4)	1.6(1.38-2.0)
Washing hand after using toilet	Yes	143	64(44.8)	1	227	79(35)	1
	No	431	228(52.9)	1.18(0.96-1.44)	315	205(65.1)	1.86(1.53-2.26)
Hygiene habits after going to the toilet	Clean by tissue	492	268(54.5)	1	326	169(51.8)	1
	Clean by water	51	14(27.5)	0.50(0.32-0.79)	107	52(48.6)	0.93(0.75-1.17)
	Both	12	4(30.8)	0.56(0.24-1.20)	73	36(49.3)	0.95(0.73-1.22)

OR(95%CI)[(2)]: *Adjusted for age and sex*

There was no association between HP infection of the studied participants and the hygiene habits such as using hand to collect food, sharing food, washing hand before eating and after going to the toilet in the Tay community. For hygiene habit after going to the toilet, people who use water to clean their bottom was half risk of having HP infection compared to those who use tissue to clean their bottom (95%CI:0.32-0.79). In the Muong, there were association between HP infection and washing hand before eating and after using the toilet, OR =1.6 (95%CI:1,38-2,0), and OR=1.86(95%CI:1.53-2.26), respectively. No association found for other habits in this group.

3.2.5. The association between Helicobacter Pylori infection and environmental hygiene conditions

Table 3.16. The association between *Helicobacter Pylori* infection in the children and environmental hygiene conditions

Environmental hygiene conditions		**Tay**			**Muong**		
		N	***HP*(+)n(%)**	OR(95%CI)[(2)]	**N**	***HP*(+)n(%)**	OR(95%CI)[(2)]
Water source	Running Well	52	11(21.2)	1	75	25(33.3)	1
	River	424	186(43.9)	2.07(1.21-3.54)	242	109(45)	1.35(0.95-1.91)
Toilet	Good	59	26(44.1)	1	177	76(42.9)	1
	Poor	407	168(41.3)	0.9(0.51-1.57)	123	53(43.1)	0.99(0.62 -1.59)
Types of house	Ceramic ground	50	24(48.0)	1	106	47(44.8)	1
	Soil ground	94	51(54.3)	1.13 (0.80-1.59)	6	5(83.3)	1.87 (1.23-2.8)
	House on stilts	146	52(35.6)	0.74 (0.51-1.06)	1	1(100)	2.25 (1.82-2.79)
Pig raising	No	167	61(36.5)	1	145	55(37.9)	1
	Yes	290	127(43.8)	1.19(0.94-1.52)	148	55(38.5)	1.01(0.75-1.35)
Dog raising	No	142	62(43.7)	1	80	32(40.0)	1
	Yes	317	127(40.0)	0.91(0.72-1.15)	214	81(37.9)	0.94(0.68-1.3)
Cat raising	No	166	71(42.7)	1	139	53(38.1)	1
	Yes	293	118(40.3)	0.94(0.75-1.17)	155	60(38.7)	1.01(0.76-1.35)

OR(95%CI)[(2)]: *Adjusted for age and sex*

There was no association between HP infection in the children and domestic animal raising or toilet conditions in both communities. Children in the families use water collected from common well, river, stream had higher prevalence of HP infection compared with those in families use water from water company (treated water) or private well (43.9% compared to 21.2% in Tay community and 45% in comparison 33.3% in Muong group). However, statistically significant difference was only found in the Tay OR=2.07 (95%CI:1.21-3.54). The Muong children in the houses with mug ground had 1.87 times higher of HP infection compared with those in the houses with brick/ceramic ground (95%CI:1.23-2,8; prevalence of 83.3% in comparison with 44.8%).

Table 3.17. The association between *Helicobacter Pylori* infection in the adults and environmental hygiene conditions

Environmental hygiene conditions		Tay			Muong		
		N	***HP*(+)n(%)**	OR(95%CI)[(2)]	**N**	***HP*(+)n(%)**	OR(95%CI)[(2)]
Water source	Running Well	75	23(30.7)	1	118	60(50.8)	1
	River	516	281(54.5)	1.77(1.25-2.51)	424	224(52.8)	1.03(0.85-1.26)
Toilet	Good	104	61(58.7)	1	353	183(51.8)	1
	Poor	476	238(50)	0.7(0.45-1.08)	180	95(52.8)	1.03(0.72-1.5)
Types of house	Ceramic ground	70	35(50)	1	186	103(55.4)	1
	Soil ground	107	62(57.9)	1.15(0.87-1.54)	7	6(85.7)	1.54(0.57-40.7)
	House on stilts	159	71(44.7)	0.89 (0.66-1.19)	4	2(50.0)	0.90 (0.33-2.42)
Pig raising	No	209	121(57.9)	1	212	108(50.9)	1
	Yes	361	174(48.2)	0.83(0.71-0.97)	247	131(53.0)	0.97(0.82-1.1)
Dog raising	No	144	76(52.8)	1	125	62(49.6)	1
	Yes	428	220(51.4)	0.97(0.81-1.16)	339	180(53.1)	1.07(0.87-1.31)
Cat raising	No	169	80(47.3)	1	201	105(52.2)	1
	Yes	403	216(53.6)	1.13(0.94-1.36)	260	135(51.9)	0.99(0.83-1.18)

OR(95%CI)[(2)]: *Adjusted for age and sex*

In the Tay community, there were associations between HP infection in the adults, and the sources of water used, and domestic pig raising. Adults used other sources of water had the risk of 1.77 time of HP infection compared to the adults used plant treated water, and private well (95%CI:1.25-2.51, prevalence of 54.5% compared to 30.7%). Adults in the households raising pig have lower risk of HP infection, OR= 0.83 (95%CI:0.71-0.97). There was not any association between HP infection in the adults and environmental hygiene conditions among the Muong ethnic group.

Table 3.18. The association between *Helicobacter Pylori* in children and socio-economic conditions

Socio-economic		Tay			Muong		
		N	***HP*(+) n(%)**	**OR(95%CI)[(2)]**	**N**	***HP*(+) n(%)**	**OR(95%CI)[(2)]**
Average income	>1milion VND	209	86 (41.1)	1	138	68 (49.3)	1
	≤1million VND	235	99 (42.1)	1.02(0.82-1.2)	151	57 (37.7)	0.62(0.39-0.99)
Occupation of mother	Farmer	268	120 (44.8)	1	107	42 (39.3)	1
	Other	33	12 (36.4)	0.75(0.35-1.6)	189	78 (41.3)	1.14(0.69-1.86)
Occupation of father	Farmer	225	82 (36.4)	1	112	51 (45.5)	1

	Other	14	10 (71.4)	4.2(1.26-14)	175	57 (32.6)	0.59(0.36-0.98)
Education level of mother	Completed high school	61	26 (42.6)	1	186	63 (33.8)	1
	Not completed high school	242	109 (45.0)	1(0.57-1.8)	142	78 (54.1)	2.61(1.61-4.31)
Education level of father	Completed high school	51	17 (33.3)	1	135	56 (41.5)	1
	Not completed high school	178	71 (39.9)	1.28(0.7-2.2)	148	47 (31.8)	0.65(0.40-1.07)

OR(95%CI)[(2)]: *Adjusted for age and sex*

For the Muong community, children living in lower income families had lower risk of HP infection compared to the children living in higher income families, OR=0.62 (95%CI:0.39-0.99; prevalence of 37.7% compared to 49.3%), while not such observation found in the Tay community. Similarly, education levels of mother was a risk factors of HP infection in their children. Children having mothers were not completed high school had 2.61 times higher risk of having HP infection compared to the children having mother were completed high school (95%CI:1.61-4.31; prevalence of 54.1%, and 33.8%, respectively). The Muong children had fathers were not farmers had 0.59 times of having HP infection compared with the children having fathers were farmers. By contrast, the Tay children having father were not farmers were 4.2 times higher than those with fathers were farmers (95%CI:1.26-14; prevalence of 42.6% compared to 71.4%). No association between HP infection in the children with education levels of their fathers or occupations of their mother in both communities.

Table 3.19. The association between *Helicobacter Pylori* in adults and socio-economic conditions

Socio-economic		**Tay**			**Muong**		
		N	***HP*(+) n(%)**	**OR(95%CI)[(2)]**	**N**	***HP*(+) n (%)**	**OR(95%CI)[(2)]**
Average income	>1milion VND	273	142(52.0)	1	227	131(57.7)	1
	≤1million VND	282	143(50.7)	0.97(0.82-1.14)	255	125(49.0)	0.84(0.71-1.0)
Occupation	Farmer	356	126(35.4)	1	530	272(51.3)	1
	Others	233	181(77.7)	0.94(0.8-1.09)	61	32(52.5)	1.01(0.79-1.31)

Education	Completed high school	239	119(49.8)	1	92	53(57.6)	1
	Not completed high school	305	163(53.4)	1.07(0.91-1.26)	480	246(51.2)	0.89(0.73-1.08)

OR(95%CI)[(2)]: *Adjusted for age and sex*

For the Tay community, no association between socio-economic factors and the risk of HP infection in the adults, while the study reported that there was statistically significant difference in HP infection between poor families (<1million VND/month) and higher income families (>1 million VND/month). People living in lower income families was lower risk of HP infection compared to its counterpart in higher income families, OR= 0.84 (95%CI:0.71-1.0).

Table 3.20. The association between *Helicobacter Pylori* in the children and crowded living condition

Socio-economic		Tay			Muong		
		N	***HP*(+)n(%)**	**OR(95%CI)[(2)]**	**N**	***HP*(+)n(%)**	**OR(95%CI)[(2)]**
Household size (m^2/person)	<20	143	54(37.8)	0.84(0.57-1.23)	127	51(40.2)	1.25(0.69-1.43)
	≥20	284	120(42.3)	1	148	67(45.3)	1
Number of people in a household	>3	78	32(41.0)	0.98(0.71-1.31)	87	45(51.7)	1.36(1.04 -1.77)
	≤3	396	165(41.7)	1	224	85(37.9)	1
Sharing bed	≤3	321	140(43.6)	1	177	67(37.9)	1
	>3	132	52(39.4)	0.9(0.7-1.15)	124	64(51.6)	1.36(1.05-1.75)
Living together (years)	1-5	38	19(50.0)	1	145	61(42.1)	1
	>5	344	147(42.7)	0.83(0.41-1.64)	92	36(39.1)	0.91(0.53-1.56)

OR(95%CI)[(2)]: *Adjusted for age and sex*

In the Muong community, children living in families with more than 3 people had higher HP infection compared to children living in families with 2 or 3 members, OR = 1.36 (95%CI:1.04-1.77; HP infection prevalence was 51.7% in comparison with 37.9%). No association between other living conditions such as household size, number of people sharing bed, and duration of living together found.

Table 3.21. The association between *Helicobacter Pylori* in the adults and crowded living condition

Socio-economic		Tay			Muong		
		N	***HP*(+)n(%)**	**OR(95%CI)[(2)]**	**N**	***HP*(+)n(%)**	**OR(95%CI)[(2)]**
	<20	262	123(46.9)	0.72(0.51-1.02)	217	123(56.7)	1.2(0.84-1.7)

Household size (m^2/person)	≥20	273	150(54.9)	1	273	142(52.0)	1
Number of people in a household	≤3	449	233(51.9)	1	352	184(52.3)	1
	>3	142	71(50.0)	0.96(0.79-1.16)	184	97(52.7)	1.0(0.85-1.19)
Sharing bed	≤3	431	132(30.6)	1	354	194(54.8)	1
	>3	123	62(50.4)	0.87(0.58-1.3)	167	74(44.3)	0.63(0.4-0.9)

OR(95%CI)[(2)]: *Adjusted for age and sex*

There was not association between HP infection in adults and the crowded living situation in the Tay. In the Muong community, there were associations between HP prevalence and the number of people sharing bed. Family having 4 people sharing bed had the risk of HP infection of 0.63 times compared with family having 2 or 3 people sharing bed (95%CI:0.4-0.9; 44,.3% against 54.8%).

3.3. The association between HLA-DQB1 gene and *Helicobacter Pylori* infection

Table 3.22. The distribution of HLA-DQB1 allele in the children by sex and history of gastro-duodenal disease of their parents

Characteristics	n	Frequency of HLA-DQB1* allele								
		0201	0301	0303	0401	0402	0403	0501	0601	0602
Sex										
Male	37	5	7	2	2	1	4	34	6	6
Female	23	0	10	8	1	1	7	10	6	4
Having father/mother had gastro-duodenal disease										
Yes	13	2	5	1	1	1	1	4	1	1
No	47	3	12	9	2	1	10	44	9	9

The prevalence of male children having HLA-DQB1*0501 allele was higher than that among female children (91,9% against 43,5%) while the prevalence of male children having HLA-DQB1 halotype 0301 and 0303 was lower than that among female children (18,9% and 5,4% against 43,5% and 34,8%). The frequency of child having HLA-DQB1 allele halotype 0301, 0303, 0403, 0501, 0601 and 0602 among children having parents with the gastro-duodenal disease much lower than the rests. All the differences are statistically significant.

Table 3.23. Distribution of HLA-DQB1 allele in the children and not *Helicobacter Pylori* infection

Allele HLA-DQB1	*HP* (+)N=30		*HP* (-)N=30		OR (95%CI)
	n	%	n	%	
0201	3	10.0	2	6.7	1.5(0.5-2.7)
0301	17	56.7	20	66.7	0.85(0.4-1.95)
0303	4	13.3	6	20.0	0.56(0.3-1.76)
0401	3	10.0	0	0	-
0402	2	6.7	0	0	-
0403	4	13.3	7	23.3	0.6(0.24-1.95)

0501	22	73.3	22	73.3	1
0601	5	16.7	7	23.3	0.67(0.33-2.93)
0602	4	13.3	6	20.0	0.56(0.3-1.76)

There is no difference of the prevalence of children carrying out HLA-DQB1 allele, halotype 0301 and 0501 between *HP*(+) *and HP*(-) groups. The appearance frequency HLA-DQB1 allele halotype 0401 and 0402 seems higher in the *HP*(+) group, meanwhile, the appearance frequency of HLA-DQB1 allele halotype 0403, 0601 and 0602 is lower in the *HP*(+) group. However, the difference is not statistically significant with p>0.05.

Table 3.24. Association between allele groups of HLA-DQB1 with *Helicobacter Pylori* infection in children

Allele HLA-DQB1	***HP*(+)N=30**		***HP* (-)N=30**		**OR (95%CI)**
	n	**%**	**n**	**%**	
DQB1*05:01//DQB1*05:01	4	12.5	9	32	0.3(0.15-0.7)
DQB1*03:01//DQB1*03:01	3	9.4	4	14	0.87(0.3-1.65)
DQB1*03:01//DQB1*05:01	10	31.3	3	11	2.56(1.04-4.76)
DQB1*03:01//DQB1*04:03	1	3.1	0	0	-
DQB1*02:01//DQB1*05:01	2	6.3	0	0	-
DQB1*03:01//DQB1*06:01/02	1	3.3	5	16.7	0.4(0.14-1.95)
DQB1*03:01//DQB1*03:02	1	3.3	0	0	-
DQB1*05:01//DQB1*06:01/02	1	3.3	0	0	-
DQB1*03:03//DQB1*05:01	1	3.3	0	0	-
DQB1*02:01//DQB1*03:01	1	3.3	1	3.1	0.98(0.76-2.87)
DQB1*02:01//DQB1*03:03/04:03	0	0	2	7	-
DQB1*03:01//DQB1*03:03/04:03	0	0	1	3.3	-
DQB1*03:01/04:03//DQB1*06:01/02	0	0	2	6.7	-
DQB1*03:03//DQB1*04:01/03	2	6.7	0	0	-
DQB1*03:01//DQB1*04:01/02	1	3.1	0	0	-
DQB1*03:03/04:03//DQB1*05:01	0	0	1	3.3	-
DQB1*06:01//DQB1*06:02	1	3.3	1	3.3	0.98(0.76-2.87)
DQB1*03:03//DQB1*04:03	0	0	1	3.3	-
DQB1*04:001/02//DQB1*04:01/03	1	3.1	0	0	-

The apperance frequency of HLA-DQB1 allele halotype 0501/0501 and 0301/0501 is the highest (21,7%). Halotype 0301/0301 and 0301/0601/02 are 11,7% and 10% respectively. There was a statistically significant difference in HLA-DQB1 halotype 0501/0501, and 0301/0501 alleles between groups of HP(+) and HP(-) with p<0.05.

Chapter 4. DISCUSSION

In the present study, the prevalence of *HP* infection in Tay people in Lang Son was 46.8% and Muong people in Hoa Binh was 48.6%. Those results are comparable to the previous studies globally. However, there was no statistically significant difference in *HP* infection prevalence between Tay and Muong people. This result supports previous studies conducted in Vietnam, including Nguyen Thi Anh Xuan (2015), and Nguyen Van Bang (2007).

Among children, the results showed that the prevalence of *HP* infection in Muong and Tay children were 42.8%, and 41.4%, respectively. The prevalence are much higher than that in developed countries like the America, and Japan. For children, the prevalence in our study were 30.9% and 32.7%, higher than that in developed countries such as Australia, and Switzerland.

Age has been mentioned as a factor determining the level of *HP* infection in many studies. The prevalence of infection tends to increase with age in the Tay (ptrend=0.00029), and Muong (p=0.0015). No statistically significant differences in *HP* infection by sex in the current study were reported.

HP infection in children commences very early. The prevalence of *HP* infection is high in children from 6 months to 3 years. This prevalence tends to increase with increasing age. The phenomenon of self-withdrawal and re-infection many times and reached the rate of 40-80% at 4-6 years old, and up to 60-85% of late adolescence (15-18 years).

There was an association between *HP* infection status in children, and their father's occupation in two ethnic groups. The associations with family income, and mother education are only found in Muong people. High education of mothers was the protective factor of *HP* infection among Muong children. Lower *HP* infection prevalence was found in the Tay children having their fathers are farmers while in Muong community, the fathers are famers was a risk factor of *HP* infection in their children.

The current study found that the Muong people living in families with better conditions are at higher risk of *HP* infection than those living in families with difficult economic conditions. These results are similar to two previous studies which was conducted in Vietnam.

The present study did not find any association between adults *HP* infection status and education levels. Studies conducted worldwide and in Vietnam (by Nguyen Van Bang, Nguyen Thi Anh Xuan, and Le Tho) showed that children had parent with low education level tended to increase *HP* infection prevalence. Results of this study also support this knowledge.

In this study, the mother's occupation was not associated with *HP* infection prevalence of their children in both communities, while the relationship with the father's profession is contradictory. Many studies in Vietnam reported that there was no association between parental occupation and *HP* infection prevalence in their children, for example studies conducted by Nguyen Thi Anh Xuan (2015) and Le Tho.

The relationship between *HP* infection, and sanitation conditions as well as eating habits is indirect evidence of the pathway theory for this bacterium such as mouth-mouth, fecal-mouth, or stomach-mouth transmission, as well as the possibility of microbial reservoirs in the nature environment. Washing hands before eating is a protective factor of *HP* infection among children in Muong community. We found that children who washed their hands before eating had a lower risk of *HP* infection than those do not have this habit among Muong community. Among the Muong adults who washed their hands before eating, and after going to the toilet had much lower risk than those who do

not. Many studies in Vietnam, and other countries has studied the hygiene habits. Similar results were reported in the study conducted by Nguyen Thi Anh Xuan in Dien Bien and Tra Vinh provinces of Vietnam.

In our study, children's eating habits included using hand to pick foods, and chewing feeding in early childhood were risk factors of *HP* infection. The results are consistent with the argument that the association between chewing feeding habits for children in childhood is a part of evidence for oral-oral *HP* transmission hypothesis.

The study could not find any association between breastfeeding period of time and *HP* infection in the studied sites. This result is similar to recent studies in Vietnam which were conducted by Nguyen Thi Anh Xuan, and Le Tho.

In order to assess the relationship between sanitation and *HP* infection, we have included variables such as the main household water source used, the kinds of toilet used, the type of dwelling house, and domestic animal raising in the analysis. We found that statistically significant differences were found only in Tay people. The associations between *HP* infection and sanitation conditions as well as eating habits are indirect evidence of these pathways of transmission such as oral-oral, fecal-oral or stomach-mouth transmission, as well as the possibility of survival of bacteria in the external environment.

The present study found no association between *HP* infection status and domestic livestock status.

Crowded living conditions are favorable conditions for *HP* transmission from human to human. In our study, crowded living condition variables were average housing area per person (number of m^2/person), household size (number of people/household), and common sleep (number of people/bed), time started to live together. The results showed that no statistically significant association between the area of the home/person, and the risk of *HP* infection among adults.

The current study demonstrated that mother has role in *HP* transmission in children. Recent studies conducted in Vietnam also support this result.

History of using antibiotics among children did not associated with *HP* infection in this study. This result are similar with previous studies conducted by Nguyen Thi Anh Xuan, Nguyen Van Bang and Le Tho.

The association between *HP* infection in children, and gastrointestinal status of their parents in both study locations was reflected in the *HP* prevalence among children with a father or a mother who is suffering from gastrointestinal disease is lower than that of parent without the disease. This result is similar to the study performed by Nguyen Van Bang that children with a history of gastrointestinal disease had a significantly higher infection rate when compared with the control group.

The study reported that in both studied populations, children with a history of allergy had a higher risk of *HP* infection, but this difference was not statistically significant. This result is similar to the results in the study of Le Tho. However, in the study of Nguyen Van Bang, children with a history of allergy had significantly higher rates of *HP* infection than children without allergies.

Association between *HP* infection and human leukocyte antigenic genotype group DQB1 (HLA-DQB1): The frequency of allele HLA-DQB1 halotype 0301, 0303, 0403, 0501, 0601, and 0602 among children in families with father/mother had gastro-duodenal disease was higher than the group which their father/mother without the disease. The difference is statistically significant, $p<0.01$. Our

results are similar to the study of Wu that the frequency of bringing HLA-DQB1 alleles halotype 0601 and 0602 was higher in those had family history of gastro-duodenal cancer.

When investigating the association between HLA-DQB1 alleles separately from *HP* infection, we found no statistically significant difference in the frequency of allele HLA-DQB1 halotype 0301, and 0501 between the two groups with and without *HP* infection.

Strengths and limitations of the study

This is the first study conducted in the Tay and Muong communities, focusing on the populous centralized location. Data, and blood sample collection were performed in each household members. The ELISA technique has been titrated on a research population of Vietnamese for high sensitivity and specificity. The study also applied modern molecular biology techniques to determine HLA genotypes. Results of the study have initially identified the HLA phenotype and genotype, however, only description was made, not yet identified the association between *HP* infection, and HLA class II. Due to costly PCR test and limited budget, the current study had limited sample size and only conducted in children but not for adults also.

HP positive cases found in this project were only announced to the health workers in the studied district health centers. Due to budget constrain, our study did not conduct any interventions, including consultation, education for lifestyle changing, and treatment for needed cases.

CONCLUSION

1. Epidemiological characteristics of *Helicobacter Pylori* infection in children aged from 6 months to 18 years, and family members of the Tay and Muong ethnic groups

The prevalence of *HP* infection among the Tay was 46.8%. Children aged from 6 months to 18 years had significantly lower *HP* prevalence than adults (41.4% versus 49.2%; OR=0.66 (0.52-0.85)). *HP* infection prevalence tends to increase with age in both children and adults (ptrend=0.000225). The *HP* infection prevalence in male was higher than that in female, and higher in boys copared to girls, however the differences were not statistically significant.

The prevalence of *HP* infection among Muong people was 48.6%. Children aged from 6 months to 18 years had lower prevalence than those over 18 years old (42.9% compared to 51.2%; OR=0.68 (0.52-0.90)). There was no difference in *HP* infection prevalence between male and female.

2. Factors associated to *Helicobacter Pylori* infection in children and household members of the Tay and Muong ethnic groups

There was a positive association between *Helicobacter Pylori* infection in children and members of the household including: age, family has *HP* infected people, hygienic and social conditions (housing ground is mug, living water source was river water, average household income of over 1 million VND/month), bad hygiene practices (chewing feeding for children, not washing hands before eating, and after going to the toilet).

3. HLA-DQB1 phenotype and association with *Helicobacter Pylori* infection in children from 6 months to 18 years

- The study identified 19 HLA-DQB1 phenotypes out of 60 serum samples tested (30 *HP* positive samples, and 30 *HP* negative samples).

- Allele HLA-DQB1*0501/0501 is the protective factor of *HP* infection while HLA-DQB1*0301/0501 allele is the risk factor of *HP* infection in children.

RECOMMENDATIONS

1. Education activities and intervention, including improving social-economic conditions, improving knowledge, strengthen hygiene practices in living and eating, to reduce the to reduce the risk of *Helicobacter Pylori* infection in children and family members of the Tay and Muong ethnic need to be performed in the Muong and Tay communities.

2. Screening and treatment for people with gastrointestinal illness who have familty member having *Helicobacter Pylori* infection, especially their parents, and siblings to avoid the transmission need to be done.

3. Futher studies about HLA-DQB1 phenotype and the association to *Helicobacter Pylori* infection should be conducted in the future.

PUBLICATIONS RELATED TO THE STUDY

1. Phan Thi Thanh Binh, Hoang Minh Viet, Nguyen Thi Viet Ha, Vu Sinh Nam (2017), "Epidemiological charcteristics of Helicobacter pylori infection among family members of the Muong ethnic in Ky Son district, Hoa Binh province", *Vietnam Journal of Preventive Medicine 2*(27), p.60-66.

2. Nguyen Thi Viet Ha, Phan Thi Thanh Binh, Vu Sinh Nam (2017), "Assessing the association between the genotype and halotype of HLA-DQB1 and H. pyloi infection in the children in Vietnam", *Vietnam Journal of Practical Medicine 5* (1043), p.113-115.

3. Thi Viet Ha Nguyen, Van Bang Nguyen, Thi Thanh Binh Phan, Thi Thu Hoang Ha, Thi Lan Anh Le and Dac Cam Phung (2016), "Epidemiology of *Helicobacter pylori* infection in Tay children in Vietnam", Annals of Clinical and Laboratory Research 4, 4(125), p.1-9.

4. Thi Viet Ha Nguyen, Van Bang Nguyen, Thi Thanh Binh Phan, Thi Lan Anh Le, Thi Thu Hoang Ha, Dac Cam Phung (2017), "Prevalence and Risk factor of *Helicobacter pylori* infection in Muong children in Vietnam", Annals of Clinical and Laboratory Research 5, 1(159), p.1-9.