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FREQUENCY OF HELICOBACTER PYLORI INFECTION USING THE HELICOBACTER PYLORI STOOL ANTIGEN TEST (HPSAT) AMONG CHILDREN DIAGNOSED WITH DYSPEPSIA.

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ABSTRACT

Objective: To determine the frequency of Helicobacter pylori infection using the Helicobacter Stool Antigen Test among children diagnosed with dyspepsia.

Study Design: Cross-sectional Study

Setting: Chong Hua Hospital and Clinics of participating pediatricians.

Study Population: Pediatric patients aged 5 to 18 years presented with abdominal pain, with or without vomiting seen at Chong Hua Hospital who consented to participate in the study were included.

Method: The HpSAT was performed in all patients and the socio-demographic and clinical profiles of children were correlated using the Spearman's rho method.

Results: HpSAT positive was seen in 10.53% (n=4) out of the 38 children who had signs and symptoms of dyspepsia. Using Spearman's rho test, statistically significant correlation were seen between HpSAT positive children and MCWD as the water source (p value=.019), intake of fruit juice (p value=.003) and history of dyspepsia in the family (p value=.050). The following had no statistical significant correlation with HpSAT positive subjects: Staying in a household of ≥ 5 members (p=.743), diet type (p=.092), effect of food intake (p=.380), acuteness of signs and symptoms (p=.576), family history of peptic ulcer disease (p=.482) and vomiting (p=.914).

Conclusion: HpSAT was positive in 10.53% of children with dyspepsia. The risk factors identified in the study that were significantly associated with H. pylori infection in children were: source of water, intake of juice and history of dyspepsia in the family. The different gastrointestinal symptomatology, particularly abdominal pain—whether acute or chronic, and its relationship to food intake and vomiting had no association in H. pylori infection. Because symptoms alone were not useful in distinguishing between causes, all aspects of the patient's evaluation--including the medical history, physical examination and laboratory review, had been essential in the diagnosis.

Keywords: H. pylori, helicobacter infections, dyspepsia, HPSAT
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INTRODUCTION

Dyspepsia is an upper, abdominal pain or discomfort that is episodic or persistent and often associated with belching, bloating, heartburn, nausea or vomiting.[1] Clinical manifestations may be acute or chronic.[1] Even though dyspepsia is a highly prevalent condition, no definitive studies had been able to establish guidelines for the work-up of dyspeptic patients in the primary care setting.[1]

Helicobacter pylori (H. pylori) infection continues to be highly prevalent in the primary care population and frequently causes gastritis and ulceration.[4] In the United States and other industrialized nations, the prevalence of infection increases about 1% each year of life until about age 50 to 60, when it stabilizes. In both industrialized and developing countries, most infections occur in childhood, usually before 5 years old.[3] Prevalence rates exceeding 50% at age 10 and 80% in adulthood had been reported.[4] Spontaneous eradication is unusual. In fact, it can persist indefinitely and it can cause severe pathology if untreated.[3] The World Health Organization (WHO) has classified H. pylori as a Group 1 (definite) human carcinogen. It can cause gastric carcinoma and mucosal associated lymphoid tissue (MALT) lymphoma in adults.[5]

This study aims to determine the frequency of Helicobacter pylori infection using the Helicobacter Stool Antigen Test among children diagnosed with dyspepsia.

SCOPE AND LIMITATION OF THE STUDY

The study only involved inpatients and outpatients at the Chong Hua Hospital and patients who were seen in the clinics of participating pediatricians, who referred them for H. pylori screening using the HpSAT, from February 1 to September 26, 2005 and based on the inclusion and exclusion criteria. A small sample size of 38 patients was enrolled in the study.

Definition of Terms

Helicobacter pylori infection: Positive for H. pylori Stool Antigen Test (HpSAT) indicated by a red line in the test region of the in vitro qualitative immunochromatographic assay by Dalle Essential Drug, Inc.

Dyspepsia: An upper, abdominal pain or discomfort that is episodic or persistent. It may be acute or chronic, and is often associated with belching, bloating, heartburn, nausea or vomiting, with no evidence of organic disease on investigation.

Chronic abdominal pain: Persistent or recurrent upper abdominal discomfort of at least 12 weeks duration, which need not be consecutive within the preceding 12 months.[25]

Acute abdominal pain: An abdominal discomfort of less than 12 weeks duration.

Peptic ulcer disease (PUD): A chronic condition, characterized by a solitary lesion—<4cm in diameter, which occurs in any portion of the gastrointestinal tract. It penetrates muscularis mucosa, may perforate gastric wall, and is diagnosed by endoscopy.[22]

Fatty meal: Refers to oily foods, *e.g.* "humba", margarine, fried foods (*i.e.* french fries, fried chicken, fried fish).

Mix meal: A meal composed of fish, meat and vegetables.

Intake of fruit juice: Refers to instant fruit juices that are commercially available. Fresh fruit juice is excluded.

Occasional fruit juice drinker: Consumes <7 glasses of juice per week.

MATERIALS AND METHODS

Study Design: Cross-sectional Study

Setting: Chong Hua Hospital, a tertiary, 600-bed capacity private hospital in Cebu City

Study Population:

Inclusion criteria

Subjects included pediatric patients aged 5 to 18 years old presented with abdominal pain, with or without vomiting, diagnosed with dyspepsia, at the Chong Hua Hospital or were seen in the private clinics of pediatricians who consented to participate in the study, from February 1 to September 26, 2005.

Exclusion criteria

The following patients were excluded:

1. Patients with concurrent diseases (e.g. pneumonia, viral infection, asthma etc.);
2. Patients with diarrhea;
3. Patients taking antibiotics and/or proton pump inhibitors less than 4 weeks at the time of examination.

Data Collection: Information on gastrointestinal symptoms, risk factors and medical history were collected from the children's parents by means of an interview conducted by the researcher and as recorded on a data form.

The stool assay used was the commercially-available, diagnostic H. pylori Antigen Rapid test (Dalle Essential Drug, Inc). It is a sandwich, solid phase, non-enzyme, immunochromatographic assay.

The study was approved by the Chong Hua Hospital Research Committee. Written informed consent was obtained from the parents of all the participants.

RESULTS

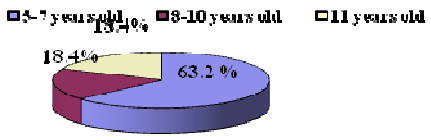
A total of 38 patients with dyspepsia were screened for H. pylori infection using the HpSAT: Twenty-four (63.2%) were 5 to 7 years old; 7 (18.4%) were 8 to 10 years old; and 7 (18.4%) were 11 years old and above (Fig. 1).

Most children screened were males (n=22, 57.9%) and 16 (42.1%) were females. Thirty (78.9%) of the children came from households with 5 to 6 members; 4 came from households with 7 to 8; and another 4 came from households with 9 or more members. Of the 38 children, majority used mineral water as source of drinking water 28 (73.7%); 10 (26.3%) used water from Metro Cebu Water District (MCWD).

According to the duration of abdominal pain, 24 (63.2%) of the patients had acute onset,

14 (36.2%) were presented with chronic abdominal pain: 20 (52.6%) of them were associated with vomiting; and 18 (47.4%) were presented solely with abdominal pain.

Figure 1. Age Distribution of Patients



Food intake had no effect on the abdominal pain in 28 (73.7%) children. Three (7.9%) subjects reported that abdominal pain was precipitated by food intake. However, 4 (10.5%) of the subjects claimed that pain was relieved after taking a meal. Only 1 (2.6%) reported that food aggravated abdominal pain. Two (5.3%) reported pain being precipitated and aggravated by food intake.

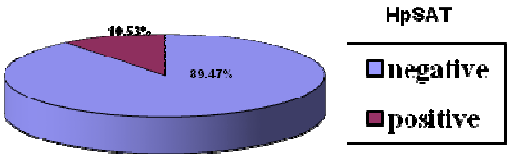
Twenty-three (60.5%) of the children usually had fatty meals. Only 15 (39.5%) had mix meals. Majority of the subjects screened were juice drinker. Children taking 2 glasses of juice per day accounted for almost half of the population (n=18, 47.4%). Eight (21.1%) of the subjects consumed 1 glass of juice per day. Three or more glasses of juice per day were drunk by 4(10.5%) subjects. Moreover, among the 38 subjects, 3 (7.9%) were occasional juice drinkers and the remaining 5 (13.2%) were non-juice drinker.

Of the 38 patients screened, only 4(10.5%) had family history of peptic ulcer disease. Twelve (31.6%), however, had positive family history of dyspepsia.

HpSAT was positive in only 4 (10.53%) of children screened. All of those who were HpSAT positive were males, 3(75%) who belonged to the 5 to 7 year old age bracket and 1 (25%) belonged to the ≥ 11 year old bracket. Correlations between sex, age and H. pylori infection were not significant at p value=0.075 and p value =0.765 respectively, according to the Spearman's rho test.

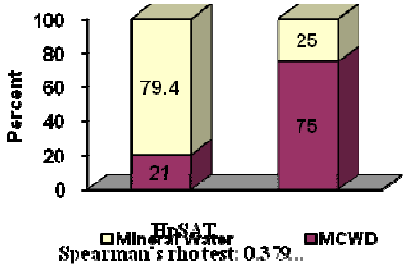
Of the 4 patients who were HpSAT positive, 3 (75%) of the subjects were from households with 5 to 6 members. One (25%) belonged to a household with ≥9 members.

Figure 2. Proportion of Patients with H. pylori Infection Using HpSAT



Three (75%) of those who were HpSAT positive used MCWD as their water source while one (25%) used mineral water (Fig. 3). This showed that the use of MCWD is significantly correlated with H. pylori infection. (P value=0.019).

Figure 3. Correlation between H. pylori Infection & Water Source



Patients positive for HpSAT were equally distributed as to duration of dyspepsia, whether acute or chronic**.**

The presence or absence of vomiting in patients positive for HpSAT was equally distributed. All patients positive for HpSAT were seen in children whose diet consisted of fatty meal, but with no statistically significant correlation with H. pylori infection**.**

The correlation of food intake and H. pylori infection in Figure 5 showed that 2 (50%) of the subjects who were HpSAT positive were children whose abdominal pain were not affected by food intake. The remaining 2 were equally distributed as to abdominal pain precipitated (n=1, 25%) and relieved (n=1, 25%) by food intake.

Figure 4. Correlation between H. pylori Infection & Duration of Dyspepsia

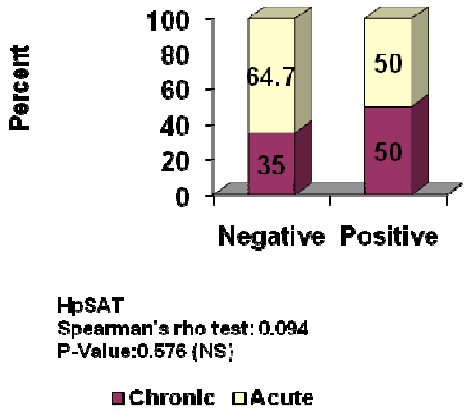
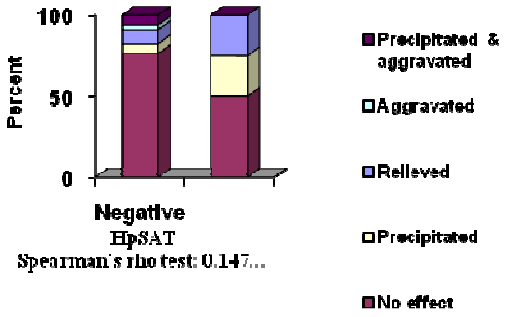


Figure 5. Correlation Between H. pylori Infection & Effects of Food Intake



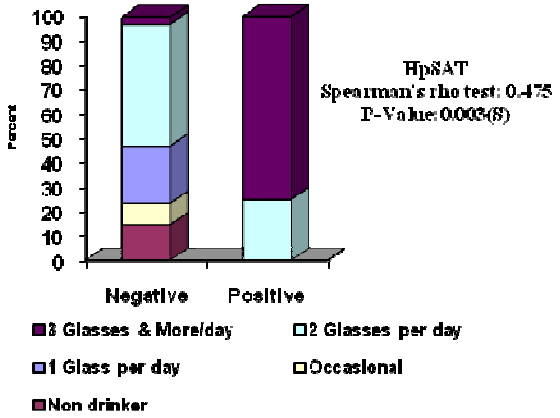
All patients who tested positive for HpSAT were those whose diet consisted of fatty meal; but this is not significantly correlated with H. pylori infection at P value= 0.380.

Three (75%) children who consumed ≥3 glasses of juice per day accounted for those who were HpSAT positive. The remaining HpSAT positive child (n=1, 25%) was one who consumed 2 glasses of juice per day. This showed significant correlation with H. pylori infection at P value= 0.003.

All patients who were HpSAT positive had family histories of peptic ulcer disease; only 3 (75%) of them had positive family histories of dyspepsia.

Using Spearman's rho test, statistically significant correlations were seen between HpSAT positive children and MCWD as the water source (p value=.019) and intake of fruit juice (p value=.003) and history of dyspepsia in the family (p value=.050). Staying in a household of ≥5 members (p value =.743), diet type (p value=.092), effect of food intake (p value=.380), acuteness of signs and symptoms (p value=.576), family history of peptic ulcer disease (p value =.482), and vomiting (p value =.914) had no statistically significant correlation with HpSAT positive subjects.

Figure 7. Correlation Between H. pylori Infection & Juice Intake



DISCUSSION

The initial evaluation of patients with dyspepsia includes a thorough history and physical examination, with special attention given to elements that suggest the presence of a serious disease. Endoscopy should be performed promptly in patients with alarm symptoms, such as melena or anorexia. Optimal management remains controversial in young patients who do not have alarm symptoms. Although management should be individualized, a cost-effective initial approach is the "Test and Treat" strategy: *e.g.* to test for H. pylori and treat the infection if the test is positive. [1]

There is a lot of controversy on the association of H. pylori infection and chronic or recurrent abdominal pain. Hafeez A, et. al. showed a significant association between chronic abdominal pains with H. pylori gastritis. [9] The same conclusion was made by SK Chong, et. al. when he showed that H. pylori gastritis was the cause of recurrent abdominal pain syndrome in children. [10] This was in contrast to the findings of the community-based case-control study done by Macarthur, et. al. who found no association between H. pylori

infection and recurrent abdominal pain in childhood.[11]

Several invasive and non-invasive tests are available to detect H. pylori infection. The invasive approach requires gastroscopy to visualize the lining of the stomach and to obtain tissue samples for histology, culture and urease test.[6] Non-invasive modalities include the 13-C urea breath test (UBT), serological test for H. pylori IgG antibodies, and more recently, a Rapid Stool Antigen test (HpSAT).[6] An ideal test for H. pylori should be non-invasive or minimally invasive, highly accurate, inexpensive, readily available, and should differentiate between active or past infection with the organism.[6]

The HpSAT is US FDA- approved for the diagnosis of active infection in symptomatic patients, like UBT and unlike serological antibody test. Furthermore, HpSAT is useful in monitoring treatment and screening of asymptomatic children. Locally, Baldomero J, et. al. conducted a study on the HpSAT using an ELISA microwell.[12] Their study included 68 adult patients who underwent gastroscopy for dyspeptic symptoms. Endoscopic findings showed gastritis in 35; gastric ulcer in 13; duodenal ulcer in 4; and combined histology in 16 patients. A rapid urease test (RUT), together with the HpSAT, was likewise done on all the patients. Using the RUT as reference standard, the investigators found that non-invasive HpSAT had a sensitivity of 91.6%, specificity of 93.7% and an accuracy rate of 92.64%. Roberto-Lucero C, et. al. also validated the use of HpSAT using the urease broth test as the gold standard, and showed sensitivity and specificity rate of 92.8% and 96.6% respectively. [13] Several foreign studies were made on the validity of HpSAT as screening test for H. pylori, and all yielded good results in favor of the use of HpSAT as replacement for the Urea breath test. The new HpSAT is a highly sensitive, specific, non-invasive diagnostic tool for the qualitative detection of H. pylori infection in children.

The study showed that of the 38 subjects, 10.53% had H. pylori infection diagnosed by HpSAT in a 7-month period. This value may be reflective of a high incidence of H. pylori infection in children.

H. pylori is now estimated to infect 2/3 of the world's population. It is acquired early in childhood, usually before 5 years of age in both industrialized and developing countries. There were more male patients.[15] It is reported that there is a 3% to 10% increase of H. pylori infection per year in children aged 2 to 8 years old in developing countries. [16]

However, the prevalence of H. pylori is not homogenous worldwide. It varies depending on the patient's chronological age, country of origin, ethnic background and socioeconomic conditions during childhood.[18] In my study, none of the HpSAT positive children had family history of peptic ulcer disease, but 75% of them had histories of dyspepsia in the family, which was statistically significant (p value=0.050). Furthermore, there was no correlation between sex and age of the patients and H. pylori infection (p value=0.075; p value=0.765 respectively). Likewise, diet type and number of household members did not also show significant correlation with H. pylori infection in children (p value=0.092; p value=0.920 respectively). Majority of patients (75%) with H. pylori infection were from the households with 5 to 6 members. Because humans are the known reservoirs of the organism, it is believed that the spread of the organism is via person-to-person transmission, including fecal-oral, oral-oral and gastric-oral routes. Hence, family overcrowding is implicated as one of the risk factors of H. pylori infection.

Fifty percent of the subjects had diets consisting mostly of fatty meals. Fatty meals are said to be risk factors for dyspepsia. [14]

Abdominal pain is the most common presentation of dyspepsia in children. It may be acute or chronic and often associated with belching, bloating, heartburn nausea or vomiting. [1] Abdominal pain was acute in 63.2% of the children, *i.e.* pain has been present for less than 12 weeks. 47.4% of the children presented only with abdominal pain while more than half of them (52.6%) had both abdominal pain and vomiting. This study showed there was no correlation between the duration of abdominal pain and H. pylori infection in children (P value=0.576). This finding is

consistent with that of Macarthur, et. al. in a community-based case-control study, which found no association between H. pylori infection and recurrent abdominal pain in childhood. [11] Bode, et. al. further concluded that abdominal symptoms provided no evidence for H. pylori infection.[7]

Interestingly, the use of the Metro Cebu Water District (MCWD) as water source showed a significant correlation with H. pylori infection (p value=0.050; p value=0.019 respectively).

The classic symptoms of peptic ulceration and epigastric pain alleviated by the ingestion of food were present only in the minority of children.[16] In my studied population, intake of food did not precipitate, aggravate, or relieve abdominal pain in almost three-fourth of the subjects (73.8%). However, intake of fruit juice was shown to be significantly correlated to H. pylori infection (p value=.003). This may be because H. pylori thrive in an acidic medium. Its acid-adaptive response enables them to grow in the acidic environment of the stomach, allowing colonization rather than just survival. Moreover, acids can break the mucosal barrier of the stomach leading to ulceration.

Juice contains citric acid and benzoic acid as preservatives. its pH level would range from 3.2 to 4.4. Eighty-seven % of the subjects were juice drinkers, with almost half of them (n=18, 47.4%) drinking an average of 2 glasses of juice per day; 21.1 % took only 1 glass of juice per day; and 10.5% took in more than 3 glasses of juice per day. Whether the amount of juice they took caused more severe signs and symptoms were not looked into in this study.

Majority of the population used mineral water for drinking. Interestingly, the use of MCWD showed a significant correlation with H. pylori infection (p value=0.019). As believed, waterborne transmission is one of the ways by which the organism is spread.

The main limitation of the study is the small sample size, and thus only a small number of patients tested positive for H. pylori. This makes it difficult to interpret the statistical tests used and only trends can be inferred. It is therefore recommended that a larger sample size be included in subsequent studies.

CONCLUSIONS

Helicobacter pylori Stool Antigen Test (HpSAT) was positive in 10.53% of the 38 children with dyspepsia, within a 7-month period.

The source of water, intake of juice and history of dyspepsia in the family showed significant correlations with H. pylori infection. These may be considered as risk factors in acquiring the infection.

Age, sex, number of household members, diet type, family history of peptic ulcer disease, and the different gastrointestinal symptomatology, particularly abdominal pain—whether acute or chronic, and its relationship to food intake and vomiting have no correlation with H. pylori infection.

Because symptoms alone were not useful in distinguishing between causes, all aspects of the patient's evaluation—including the medical history, physical examination and laboratory review, were essential in the diagnosis. Furthermore, the very small proportion of patients who tested positive for HPSAT due to the small sample size made this study inconclusive.

RECOMMENDATIONS

Due to the limitations of this study, the following are recommended for future investigation: To increase sample size and extend period of investigation; To include patients admitted in other hospitals in our locality; and to conduct further investigation in all age groups, including those who are asymptomatic.

REFERENCES

1. Bazaldua O, PHARM. D., Schneider F, M.D. M.S.P.H. Evaluation and Management of Dyspepsia. American Family Physician. 1999; 60:1773-88.
2. Braden B, Hans-George P, Ahrens P, Kitz R, Dietrich CF, Caspary W. New Immunoassay in Stool Provides an Accurate Noninvasive Diagnostic Method for Helicobacter pylori Screening in Children. Pediatrics. 2000; 106(1)
3. Sanchez IL. H. pylori Infection and abdominal pain. The Philippine Journal of Pediatrics. Philippine International Convention Center, Pasay City. April 7-10, 2002; 86-88.
4. Bonagura AF, Dabezies MA. Helicobacter pylori infection-The importance of Eradication in Patients with Gastric Disease. Post graduate medicine. 1996; 100(5).

5. Working Group on H. pylori infections in Children and Adolescent. World Congress of Pediatric Gastroenterology and Nutrition. August 5-9, 2000. Boston, Mass. USA.
6. Lippincott Williams and Wilkins Inc. Helicobacter pylori Infection in Children: Recommendation for diagnosis and treatment. Journal of Pediatric Gastroenterology and Nutrition. November, 2000; 490-497.
7. Bode G., Rothenbacher D.,Brener H., Adler G. Helicobacter pylori and Abdominal Symptoms: A population-based Study among Pre-schooler Children in Southern Germany. Pediatrics. 998; 161: 634-637.
8. Ganga-Zandzou, Michaud I., Vincent P et al. Nocturnal outcome of Helicobacter pylori Infection in Asymptomatic Children: A two-year follow up study. Pediatrics. 1999; 104:216-221.
9. Hafeez A, Ali HS. Recurrent Abdominal Pain and Helicobacter pylori infection in Children. JPak Med Assoc. May, 1999; 49 (5): 112-4
10. Chong SK, Lou Q, Asnicar MA, Zimmerman SE, Croffie JM, Lee CH, Fitzgerald JF. Department of Pediatric, Gastroenterology and Nutrition. James Whitomb Riley Hospital for Children, Indiana University School.
11. MacArthur C. Helicobacter Pylori, Non ulcer Dyspepsia and Childhood Recurrent Abdominal Pain. International Pediatric Research Foundation, Inc. 2001;49:140.
12.. Baldomero JG, Caballero R, Tan JA, Gonzales B. Rapid Detection of Helicobacter pylori Antigen in Stool Specimen using a non invasive enzyme immunoassay. United doctors Medical Center, unpublished
13. Roberto-Lucero C, Gloria VI, Zano, Banez VP, Nolasco ER, Daez ML. Stool Antigen Test: A Noninvasive detection of Helicobacter pylori infection. University of the Philippines, PGH Section of Gastroenterology. unpublished
14. Bherman RE, Kleigman RM, Jenson HB. Peptic Ulcer Disease. Nelson Textbook of Pediatrics, 17th edition. Chapter 316, pp1245-1247.
15. Parsonnet J. The incidence of *Helicobacter pylori* infection. *Aliment Pharmacol Ther.* 1995;9:45–51.
16. Kato S, Sherman PM. What is New Related to Helicobacter pylori Infection in Children and Teenagers? Archives of Pediatrics and Adolescent Medicine. Vol.159 No.5, May 2005; 159: 415-421.
17. Marcus EA, et. al. Acid Adaptive genes of Helicobacter pylori. American Society of Microbiology. Infection and Immunity (IAI), Vol. 71, No. 10. October 2003; pp 5921-5939.
18. Cotran RS, Kumar V, Robbins S. Gastric Ulceration. Robin's Pathologic Basics of Disease. Chapter 17. The Gastrointestinal Tract. pp 773-777.
19. Drumm B, Sherman P. Gastritis in Childhood. Pediatric Gastrointestinal Disease.Vol.1, Chapter 26, part 2; pp 426-435.
20. Marshall BJ. Helicobacter pylori. AmJ Gastroenterology 1994; 89: S16-28.
21. Loening-Baucke, Vera, M.D. Dyspepsia in Children. Digestive Health Matters, Vol. 2, No 3. Fall 2000.
23. MacArthur C, Saunders N, Feldman W, Ipp M, Lee PW, Roberts S, Best L, Sherman P, Pencharz P, Zanten, SV. Helicobacter pylori and Childhood Recurrent Abdominal Pain. Community based case-control study. BMJ 1999; 319:822-823.