

The effect of dairy products on the therapeutic regimen of patients with *Helicobacter pylori* infection in Aden, Yemen

Nashwan Saleh Mohammed

Al-Nasr general hospital and Al ashwal clinic for Medical & Cardiac Diseases Adhala || Yemen

Abstract: Aim: To determine the effect of intake of dairy products on therapeutic regimen of patients with *Helicobacter pylori* (*H. pylori*) infection in Aden, Yemen.

Methods: A observational study based on questionnaire and ultrasound imaging. MS Excel was used for data entry and analysis. Ethical concerns done as required including consent forms and acceptance of participants to be involve in the current study.

Sample and Sampling: Study sample was consisted of 1300 patients (1000) females and (300) males with confirmed *H. pylori* history were recruited using a purposeful, non-random sampling.

Results: Manifestations and laboratory results revealed 1296 patients with *H. Pylori* infection treated within one week by triple regime (Amoxicillin 500mg, Clarithromycin 250 mg and Lansoprazole 30 mg every 12 hours daily for 14 days) with complete prohibition of diary intake, while 4 female patients not strictly stopped consumption of dairy products that failed in eradication of *H. pylori* infection upon laboratory results. Patients whom not involved in complete restriction of diary intake and given the triple regime get treated after 81 days. Also, patients with Positive *H. Pylori* Ag in stool samples of the previously treated patients reappeared after re-used of dairy products.

In conclusion *H. Pylori* seriousness represented by its mode of transmission through the food; milk and dairy products. Consumption of dairy products has a negative effect on therapeutic regimen of patients with *Helicobacter pylori* infection.

Keywords: Dairy products, *Helicobacter pylori*, infection, triple regime Yemen.

Introduction:

Helicobacter pylori is a gram-negative spiral bacteria colonize the gastric antrum [1] and the intestinal tract [2], it is a bacteria of numerous strains with two subtypes (Cag A+ and Cag A-) [3,4]. Human *H. Pylori* infections produce symptomatic and asymptomatic pt.'s [5,6], according to the strain subtype (Cag A+ or Cag A-).

It can be diagnosed by [7,8,9,10,11,12] rapid urease-breath test (by help of gastro endoscope), anti-CagA specific antibodies (anti-CagA IgG, IgE, IgM and IgA), anti-*H.pylori* IgG, histological biopsy and culture, anti-*H.pylori* mucosal IgA [13,14], and *H. Pylori* antigen in stool [15,16]. The urease is the enzyme that catalyzes the hydrolysis of urea to ammonia and Carbon dioxide [17]. Thus *H. Pylori* urease neutralizes the acidic medium permitting its survival in the stomach.

Recent studies trying to explore the relationship between H. pylori infection and dietary behaviors personal preferences, ethnic heritage and tradition, habit, economy, social interactions, and emotional relief and stability [2,3].

Many studies showed that H. pylori infection is the most common bacterial infection, exceeds 50% of the world's population in general and Palestine in particular as well [4]. H. pylori infection is the primary cause of peptic ulcer disease and an etiologic agent in the development of gastric cancer [1,3]. In addition the H. pylori infection is related to many diseases as diabetes, hypertension, ovarian polycystic disease and other diseases. Also, previous studies showed there is relationship between dietary factors, lifestyle, socioeconomic status and H. pylori contagion [5].

For that, verification of the transmitted source for the H. Pylori bacteria by clinical and para clinical study is a must to get a protection from the infection with its long morbidity and high mortality.

Based on non-published study created in 2006 by the author that included 390 patients male and female formed two groups the first one's was the obliged for the orders of prevention from using the milk and dairy products and whom patients for that succeeded in H. Pylori eradication with negative result of H. Pylori antigen(Ag) in their stool tests by the serological CTK Biotech cassettes after two weeks treatments by amoxicillin 500mg, clarithromycin 500mg and lansoprazole 30mg every 12 hours while the other group's formed of 152 male and female used the same therapeutic regime but not obliged therefore not succeeded.

We decided to conduct the current study that aimed determine the effect of intake of dairy products on therapeutic regimen of patients with Helicobacter pylori (H. pylori) infection in Aden, Yemen.

Materials and Methods

Methods: An observational study based on questionnaire and ultrasound imaging. MS Excel was used for data entry and analysis. Ethical concerns done as required including consent forms and acceptance of participants to be involve in the current study.

Sample and Sampling: Study sample was consisted of 1300 patients (1000 females and 300 males with approved H. pylori history were recruited using a purposeful, non-random sampling.

The Test- Result method was used for the study by using the serological survey for the detection of H. Pylori antigen that depend on the reaction of the excreted substances in the stool with the cassette antibodies such as Spin react (Spin- helicobacter pylori antigen in stool), Acro-biotech (helicobacter pylori antigen and antibodies) plus clinical correlations of the patients manifestation pre and post treatment to avoid the disadvantage of false negative due to low concentration of the antigen which was solved by using centrifuged samples of stool. Stool antigen test considered alternative to urea breath test for detection and follow-up

(before and after treatment evaluations) [28] with avoidance of the drugs that may decrease the accuracy of the result such as acetyl cysteine.

Then prescription of treatments was done for triple regime of low doses (clarithromycin 250mg + amoxicillin500mg + lansoprazole30mg) daily every 12 hours for 7 days only, and every other day or with need there was a phone contact to explained any sufferings and gave a direction to them. And investigation of stool H. Pylori antigen to detect a new infection alongside the follow-up periods on 7,14,30,60 and 81 days of the prevention from the use of the marketing pasteurized milk and dairy products or any food or fluid contained it was done.

Twenty cases of the patients from the obliged group's, Re- used the marketing pasteurized milk and dairy products for 7-14 days after the 81 days, Aimed to see the result of the stool H. Pylori antigen after negative one at the day 81.

Results:

Figure 1 of study conducted in 2006 that shown a relation between the milk and dairy products and preserved positive H. Pylori antigen in stool sample, represented the two groups the first consist of 138 females and 100 males obliged the ordered and succeeded in H. Pylori eradication to become zero that mean no patient's with H. Pylori while the other group's consist of 100 female and 52 male no obliged the ordered and therefore failed to eradicated the H. Pylori bacteria (preserved positive H. Pylori Ag in stool).

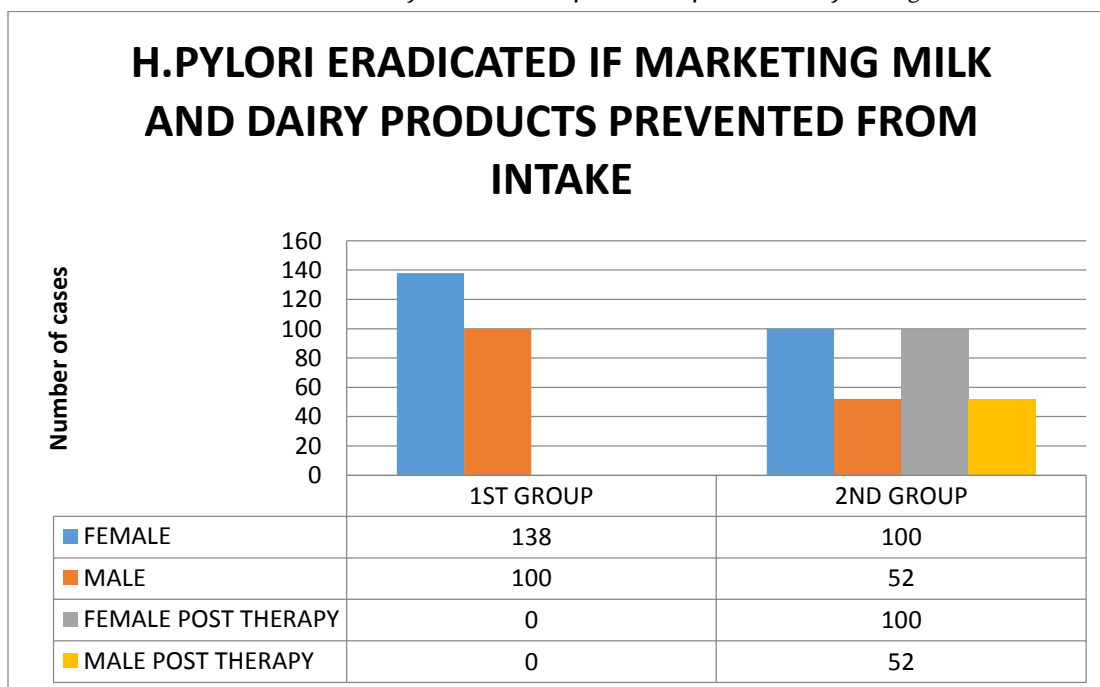


Figure (1) Milk and dairy products prevention help in eradication of H. Pylori infection.

The results shown in Figure 1 encouraged the authors to conduct the current study to find relationship between the milk substance and the drugs, but when some of the patients in the obliged group that got a negative stool result after successful therapy were returned after 20 days with the same symptoms and their investigation of stool samples again revealed a positive result because they were re-used a pasteurized milk, yogurt, cream, tea- milk, chocolates with milk post successful treatment.

Figure 2 shown the relation between the market pasteurized milk and dairy products and the H. Pylori bacterial infection among participants, the number of patients was 1300 from them 1000 female and 300 male was prevented from the intake of the milk or any type of dairy products for a period of 81 days from the first day of diagnosis, all of obliged patients to milk restriction were succeeded in eradicate the H. Pylori antigen (1296 male and female patients) and the non-obliged patients were (only 4 female) who failed to eradicate the H. Pylori bacteria.

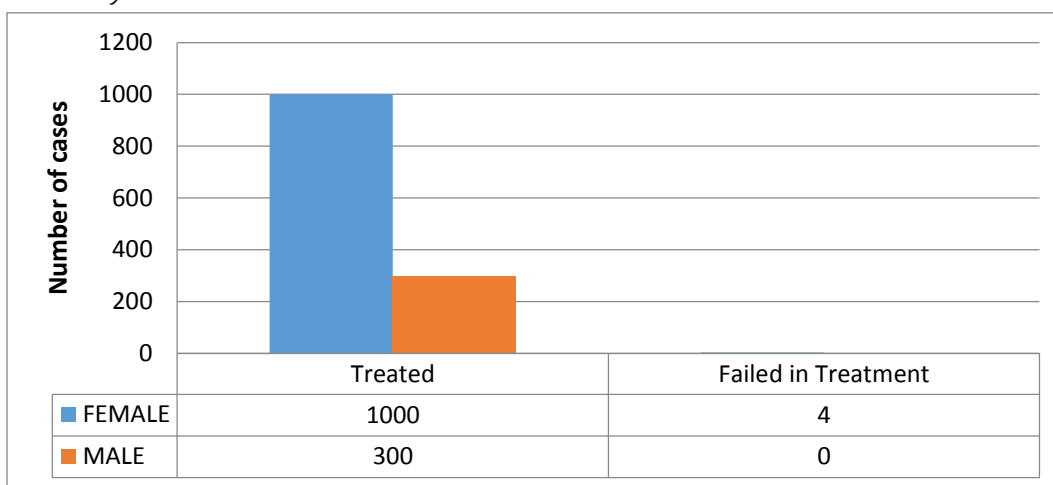


Figure (2) Avoidance of market pasteurized milk and dairy products prevent the H. Pylori infection.

Represent the group under study (1000 female and 300 male) all of them (1296 pt.'s =99.7%) treated from H. Pylori bacteria within one week in absence of the marketing milk and dairy products ,except for (4 female=0.3%) cases not strictly obeyed the orders.

The successful eradication of H. Pylori infection was successful by correlation of the improvements in the patient’s manifestations (as explained by the table No.1 and figure No.3) by the pre-therapeutic investigation and post therapeutic investigation.

Table (1) Clinical manifestation of pt.'s with H. Pylori infection pre and post treatment.

Clinical manifestations.	Pretreatment	Post treatment
	% (n)	% (n)
Epigastric burning.	90% (1170)	65% (845)
Post feeding	86% (1118)	63% (819)
Pre feeding	4% (52)	2% (26)
Abdominal distension	100% (1300)	30% (390)
Right para umbilical	87% (1131)	20% (260)
Left para umbilical	13% (169)	10% (130)
Abdominal sounds	87% (1131)	5% (65)
Tongue discoloration	97% (1261)	97% (1261)
Bad breathing	3% (39)	0% (0)
Chest pain(intermittent)	35% (455)	45% (585)
Right subcostal pain and tenderness	100% (1300)	100% (1300)
Anterior neck pain and tenderness	25% (325)	100% (1300)
Body ache	60% (780)	100% (1300)
Axillary pain	3% (39)	3% (39)
Obsessive thoughts	0.23% (6)	0% (0)

Figure No (3) explained the improvements in epigastric burning (pre and post therapy), abdominal distension, abdominal sounds, bad breath and obsessive thoughts manifestations and almost all of them stopped the use of the proton pump inhibitors like omeprazole, lansoprazole...etc., due to the subsided hyperacidity and the remainder epigastric burning actually was due to inflammatory process in the fibromuscular and in the gastric walls that relived only by anti-inflammatory drugs.

The results of the re-used milk and dairy products (as explained in the figure No.4) by the 20 patients that were succeeded to eradicate H. Pylori infection after their abstinence of using it along the researched period became the appearance of positive H. Pylori antigen in stool after 7-15 days of re-using.

20 patients (14 female;20-30 yrs. Old, and 6 males;16-25yrs old) that re suffered from the previous gastric symptoms and their stool tests revealed positive H. Pylori antigen mean returned infection.

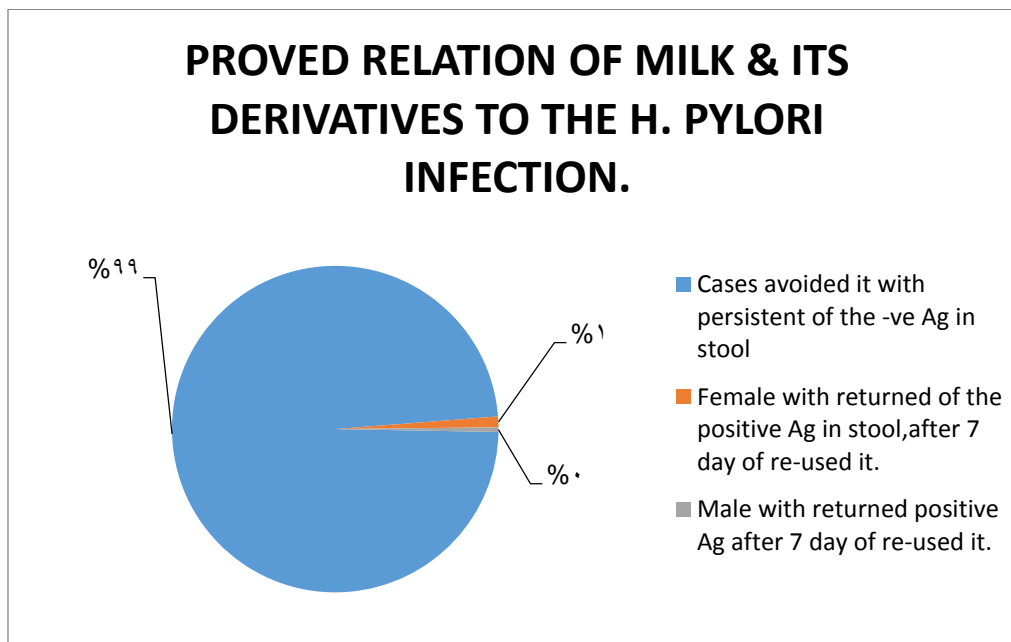


Figure (4) The milk and dairy products are the cause of re-infection by H. Pylori bacteria.

Represent the cases that avoided the marketing milk and dairy products with success of h. Pylori eradication (1296 case of male and female) and the cases that re-used it (20case of 14 female and 6 male) were again re infected by returned the positive H. Pylori Ag in stool after negative one.

Discussion

Milk is one of the best means for survival of H. Pylori bacteria due to its high ph. That helping the bacteria to pass the acidic barrier of the stomach to reach the layer of sub mucosa to begin its growing phase. Some studies have reported the presence and survival of H. pylori in dairy products [18]. Fujimura et al showed that the prevalence of H. pylori was 50% in cow feces and 38% in soil samples. Contact with cow feces and soil is the main source of milk contamination. Milk could also be contaminated during production or because of the inadequate processing hygienic management of the product, which could transmit the bacteria to humans, they found the ureA gene of H. pylori in 13 out of 18 (72.2%) raw milk samples and in 11 out of 20 (55%) commercial pasteurized milk samples [19]. Azevedo et al could not prove the existence of H. pylori in milk through culturing. These findings are very important to explain the way of transmission of H. pylori to humans through milk and food [20]. Fujimura et al. reported that H. pylori might not be cultured in pasteurized cow's milk because it might be changed to a coccoid form through pasteurization [21]. Wang et al. and Orozco et al. showed a progressive decrease in bacterial load with an average survival of nine days in pasteurized milk and 12 days in UHT milk, with an estimated average of original inoculums of 105 and 106 cfu/ml. Other studies were unable to pick up H. pylori from the culture of pasteurized milk [22]. Anti H. pylori

effects in milk might damage *H. pylori* and inactivate a non-culturable state that inhibits its multiplication in culture media [23,24]. *H. Pylori* changes in three different forms under environmental stress: first, viable spiral forms that are culturable, virulent, and infectious and induce inflammation in experimental animals; second, inviable coccoid forms that are nonculturable, less virulent, and less likely to colonize and induce inflammation in experimental animals; and a third form that is a nonviable degenerative form of dying *H. pylori* [25].

Milk and dairy products are the mode of *H. Pylori* bacterial transmission to humans by the guide of resultant positive stool *H. Pylori* antigen after 7-10 days of tea milk, yogurt, cream intake, and positive Rapid-Urease Test by help of gastro endoscopic biopsy after 20 days of milk ingestion.

In opposite to that from clinical view the inviable coccoid forms of the *H. Pylori* bacteria that may be present in the treated sewerage water were flared the patients manifestations as seen from the patients that re-used the offenders, mean the coccoid forms either converted to viable form or its parts stimulating the autoimmune process. Improvements in the patients suffering and the resultant negative *H. Pylori* antigen in stools samples after anti- *H. Pylori* therapy due to positive *H. Pylori* antigen in the stool of the same patients in pretreatment period, beside the preservation of the negative stool results along the follow-up period 81 days. Recurrence of the positive *H. Pylori* antigen in stool samples after re-using a milk and dairy products for near 20 days, after their success in its eradication and preservation of negative results for 5 times during the treatment and follow- up periods. The current study, coincided with the studies previously mentioned and concluded that *H. Pylori* Ag presented in commercial pasteurized milk and raw cow's milk examined by PCR ELISA KIT of milk serum while my study focused on the compares between the clinical and para clinical results in the pre and post therapeutic periods, concluding that, even if there is inhibitory substances for detection of the *H. Pylori* antigen by laboratory tests from the milk products directly it will be removed by the digestion of the milk and helicobacter forms (spores or coccoid) will accommodate on the new living conditions in the gastric sub mucosa and converted from the coccoid form(resistible and dormant) to the flagellated penetrating one's.

Therefore I consider the marketing milk and dairy products a first offender in human infection because it's the best medium that can preserve the life of the *H. Pylori* bacteria due its contents (nutrients, especially the small amount of the urea and proteins and the high ph.(5.5-6.7)and because it's the only fluid that has the ability to increase the stomach PH returned it less acidity, And abolished the defensive acidic medium to permit for the entrance of the *H. Pylori* bacteria to the sub mucous layer and completing its adhesion, that was explained by the need to large numbers(10⁶) of any bacteria [26] to cause an infection in

presence of acidic medium to pass through the gastric to the intestine in between the foods layers, but to stay in the gastric this needed a help which given by the milk and dairy products .

Why it's the offender? Because it's the only fluid after the water and beverages that used by everyone of different age groups in the world and it is proved by this study the re-infection by positive H. Pylori antigen of the patients re-used the milk or dairy products.

The H. Pylori bacteria discharges from the cows in the milk or the contaminated milk during collection or processing? In our country, in places near the chicken's farms in Ad Dala-Yemen the cattle and cows left to feed on the chickens feces(stool) to get a high weight and gave them a large quantity of milk caused infection for those people who drank it or ate a food mixed with it.

Conclusion

H. Pylori seriousness represented by its mode of transmission through the food; milk and dairy products. Consumption of dairy products has a negative effect on therapeutic regimen of patients with Helicobacter pylori infection.

Acknowledgements:

Greatest thanks to all the patients that trusted in me in spite of theirs suffering to leave their liked food, and all of that was due to chronicity of the manifestations which took them to every clinic with no benefits, and to my wife who was one of them given me the enforcement to complete this works, greatest thanks to Dr. Arafat Abdu, College of Medicine, Microbiology Department, Aden University, Also I hope to the Countess Nabilla to accept my greatest thanks for the directory points. (At the end I hope to solve this catastrophe).

References:

- 1- Atherton J. The pathogenesis of H. pylori–induced gastro-duodenal diseases. Annu. Rev. Pathol. 2006 1:63-96
- 2- Parsonnet, J., D.Vandersteen, J. Goates, R. K. Sibley, J. Pritiken, and Y. Chang. Helicobacter pylori infection in intestinal-and diffuse-type gastric adenocarcinomas. J. Natl. Cancer Inst. 1991; 83:640-643.
- 3- WeelJFL,van der Hulst RWM,Gerrits Y,et al. The interrelationship between cytotoxin-associated gene A, vacuolating cytotoxin, and Helicobacter pylori-related diseases. J Infect Dis 1996;173:1171±5.
- 4- Jaferzadeh et al. Prevalence of anti-H. pylori antibodies. JRMS 2006; 11(5): 285-291
- 5- Megraud F. Epidemiology of Helicobacter pylori infection: where are we in 1995? Eur J Gastroenterol Hepatol 1995; 7: 292-5.

- 6- Epidemiology of, and risk factors for, *Helicobacter pylori* infection among 3194 asymptomatic subjects in 17 populations. The EUROGAST Study Group. *Gut* 1993; 34(12):1672-1676.
- 7- Calvet X, Sánchez-Delgado J, Montserrat A, et al. Accuracy of diagnostic tests for *Helicobacter pylori*: a reappraisal. *Clin Infect Dis* 2009;48:1385-91.
- 8- Al-Humayed SM, Ahmed ME, Bello CS, et al. laboratory methods for detection of *Helicobacter pylori*. *Saudi Med J* 2008;29:530-2.
- 9- Redéen S, Petersson F, Törnkrantz E, et al. Reliability of Diagnostic Tests for *Helicobacter pylori* Infection. *Gastroenterol Res Pract* 2011;2011:940650.
- 10- Vaira D, Perna F. How useful is the rapid urease test for evaluating the success of *Helicobacter pylori* eradication therapy? *Nat Clin Pract Gastroenterol Hepatol* 2007;4:600-1.
- 11- Uotani T, Graham DY. Diagnosis of *Helicobacter pylori* using the rapid urease test. *Ann Transl Med*. 2015 Jan;3(1):9.
- 12- Yousfi MM, El-Zimaity HM, Cole RA, et al. Detection of *Helicobacter pylori* by rapid urease tests: is biopsy size a critical variable? *Gastro Intest Endosc* 1996;43:222-4
- 13- Pefia AS, Endtz HPh, Offerhaus GJA, Hoogenboom-Verde-gaal A, van Duijn W, de Vargas N, et al. Value of serology (ELISA and immunoblotting) for the diagnosis of *Campylobacter pylori* infection. *Digestion* 1989;44:131-41.
- 14- Crabtree JE, Taylor JD, Wyatt JI, et al. Mucosal IgA recognition of *Helicobacter pylori* 120 kDa protein, peptic ulceration, and gastric pathology. *Lancet* 1991;338:332-5.
- 15- Duck M, Wang Y. Stool antigen assay can effectively screen *Helicobacter pylori* infection. *Gastroenterology*, 2001 5: 98-103.
- 16- Forné M, Domínguez J, Fernández-Bañares F, Lite J, Esteve M, Galí N, Espinós JC, Quintana S, Viver JM, Accuracy of an enzyme for the detection of *Helicobacter pylori* in stool specimens in the diagnosis of infection and posttreatment check-up. *Am J Gastroenterol* 2000, 95:2200-2205.
- 17- Scott DR, Marcus EA, Weeks DL, Sachs G. Mechanisms of acid resistance due to the urease system of *Helicobacter pylori*. *Gastroenterology*. 2002;123:187–95.
- 18- Brown LM. *Helicobacter pylori*: epidemiology and routes of transmission. *Epidemiol Rev* 2000; 22(2): 283-97.
- 19- Fujimura S, Kawamura T, Kato S, Tateno H, Watanabe A. Detection of *Helicobacter pylori* in cow's milk. *Lett Appl Microbiol* 2002; 35(6): 504-7.

- 20- Azevedo NF, Guimaraes N, Figueiredo C, Keevil CW, Vieira MJ. A new model for the transmission of *Helicobacter pylori*: role of environmental reservoirs as gene pools to increase strain diversity. *Crit Rev Microbiol* 2007; 33(3): 157-69.
- 21- Ghasemian Safaei et al. *Helicobacter pylori* antigen in Milk and Feces. *JRMS* 2011; 16(2):184-187.
- 22- Wang X, Hirno S, Willen R, Wadstrom T. Inhibition of *Helicobacter pylori* infection by bovine milk glycoconjugates in a BALB/cA mouse model. *J Med Microbiol* 2001; 50(5): 430-5.
- 23- Orozco A, Ogura T, Hirosawa T, Garduno R, Kubo I. In hydrolyzed cow's milk *Helicobacter pylori* becomes nonculturable and the growth of *Salmonella typhi* and *Escherichia coli* is inhibited. *J Food Sci* 2007; 72(8): M306-9.
- 24- Oliver JD. The viable but non culturable state in bacteria. *J Microbiol* 2005; 43(Spec No): 93-1
- 25- Fan XJ,, Chua A, Shahi CN, Devitt JMC, Keeling PWN, Kelleher D, Gastric . lymphocyte responses to *Helicobacter pylori* in patients with H. pylori colonization. *Journal. Gut. BMJ.* 1994;35:1379-1384
- 26- Howden and Hunt Relationship between gastric secretion and infection. *Gut.* 1987; 28: 96-107

تأثير تناول منتجات الألبان على النظام العلاجي لمرضى الإصابة بالبكتيريا الحلزونية البوابية في عدن، اليمن

المخلص: هدف البحث إلى تحديد أثر تناول منتجات الألبان على النظام العلاجي للمرضى المصابين بعدوى بكتيريا الملوية البوابية في عدن، اليمن.

وتم استخدام منهج البحث الوصفي على أساس الاستبيان. حيث تم استخدام MS Excel لإدخال البيانات وتحليلها. الاهتمامات الأخلاقية القيام به على النحو المطلوب بما في ذلك أشكال الموافقة وقبول المشاركين المشاركة في الدراسة الحالية. وتألقت عينة الدراسة من 1300 مريض (1000 أنثى و300 ذكراً) وكانت العينة هادفة وغير عشوائية.

النتائج: كشفت المظاهر ونتائج المختبر أن عدد (1296) مريضاً بالعدوى بالبكتيريا الحلزونية المعالجة في غضون أسبوع واحد عن طريق نظام العلاج ثلاثي (أموكسيسيلين 500 ملغ، كلاريثروميسين 250 ملغ وانسوبرازول 30 ميلي غرام كل 12 ساعة يوميا لمدة 14 يوماً) مع الحظر الكامل لتناول منتجات الألبان. في حين 4 من المرضى الإناث لم يمنعو بشكل فعال من استهلاك منتجات الألبان خلال فترة العلاج مما أدى إلى فشل القضاء على عدوى هليكوباكتر بيلوري. وتم علاج المرضى الذين لم يتقيدوا بالتوقف عن تناول منتجات الألبان خلال علاج عدوى هليكوباكتر بيلوري باستخدام النظام الثلاثي بعد 81 يوماً

الخلاصة: تنتقل بكتريا هليكوباكتر بيلوري من خلال الغذاء خاصة الحليب ومنتجات الألبان. وكان لاستهلاك منتجات الألبان تأثير سلبي على النظام العلاجي للمرضى المصابين بعدوى هليكوباكتر بيلوري.

الكلمات المفتاحية: منتجات الألبان. هليكوباكتر بيلوري. عدوى، نظام العلاج الثلاثي، اليمن.