Comparison of the Helicobacter Pylori Diagnosis Methods with Analytic Network Process

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Abstract - **Helicobacter pylori is infecting %70-80 of the world's population and is assumed to cause gastric diseases. Diagnosis of the bacteria is crucial for the treatment of the bacteria related infections. Histology, culture, urea breath test, stool antigen test some of the diagnosis methods each having specific strength and weaknesses as sensitivity, specificity, cost, easiness, time, effectiveness in the treatment and laboratory requirements. In this study, three of the commonly used H. pylori diagnosis methods: histology, culture and urea breath test, are evaluated with Analytic network process (ANP) and the rank of the criteria and alternatives are obtained. The evaluation of the methods and the rank of the diagnosis methods can reduce time, cost, and validity of the test results.**

Keywords - **Helicobacter Pylori, Invasive Diagnosis Methods, Non-Invasive Diagnosis Methods, Analytic Network Process (ANP).**

1. Introduction

Helicobacter pylori is a bacteria which is assumed to cause peptic ulcer, MALT,lenfumal gastric and gastric cancer. The world's populationis %50 and the developing countries %70-80 is infected with this bacteria. The bacteria have around 20 different variants. Among these variants especially 3-4 types are hazardous[1].

In developing countries, the most common way of transmission of H. pylori is by either the oral-oral or fecal-oral route[2]. Commonly, H. pylori is transmitted person-to-person by saliva but the isolated bacteria from feces, saliva and dental plaque showed that bacteria can be more easily transmitted via gastric mucus than via salvia. No evidence could be found for the transmission of the bacteria from animals to humans [3], [4].

The diagnosis of the H.pylori can be done with methods as "rapid urease test, histology, culture, urea breathe test, stool antigen test, blood-based tests (serology) , each having different attributes and require specific technology and skills. The selection of the diagnosis method is a multi-criteria decision making method (MCDM).In order to make consistent comparisons among the alternatives, Analytic network process is applied to the selection process.

2. Diagnosis of Helicobacter Pylori

For the diagnosis of H. pylori infection there are several both invasive and non-invasive methods[5]. The choice between different methods is dependent on the clinical situation and if gastroscopy is needed[5]. No single method can be considered to be ideal for the detection of H. pylori infection. On the other hand, the cost-effectiveness of the different diagnostic strategies is based on the prevalence of the infection and on the price and accuracy of different tests[6].

The accuracy of all diagnostic tests described for the detection of H. pylori infection depends on the clinical situation in which they are used. Especially in settings with a low prevalence of H. pylori infection even tests with high sensitivity and specificity may turn out to give low positive predictive values and this should be taken into account when these tests are used [7].

2.1. Invasive Diagnosis Methods

The methods need gastric biopsy material taken by *gastroscopy* from the *antrum* and *corpus* of the host which provides better chance of successfully culturing the organism [8].The possibility of false negative results due to sampling error can be minimized by sophisticated experience.

To access a better yield, the patient should have undergone several weeks without taking antibiotics or *antisecretory* drugs such as proton pump inhibitors (PPI) and *omeprazole*[9].

Invasive methods are suggested if the cancer prevalence is high and if the patient is over 45 years in order to detect degree and type of mucosal damage.

Invasive methods are "**Rapid urease test, Histology, Culture and antimicrobial susceptibility and Molecular methods (PCR)"**[10]**.**

- **Rapid urease test**is done by the mucosa taken from the antrum of the stomach. The mucosa is placed in a medium containing urea enzyme where the H.pylori hydrolyzes the urea to ammonia and in turn changes the color of the specimen from yellow (NEGATIVE) to red (POSITIVE[11].The reading of the color should be done in 24 hours. False negatives are possible by urease producing bacteria from oral activity[12].

- **Histology** is the microscopic analysis of the gastriccells and tissues. The diagnosis of the gastric cancer requires histopathological examination. There is a need for sophisticated laboratory and trained physicians[13].

- **Culture** is the most specific method for diagnosis. The method is difficult since isolation of transportation and culture environment from external environment needs care. Culture is preferred for the determination of the antibiotic sensitivity of the H.pylori strains[14].

2.2. Noninvasive Diagnosis Methods

Noninvasive methods are based on serum, stool, urine, or saliva specimens. **"Ureabreathe test (UBT),stool antigen test, and blood-based tests (serology)**" are noninvasive tests[15].

- **Urea breathe test** is the standard non-invasive test for H.pylori detection with highest accuracy. The method depends on the determination of the labeled carbon dioxide in the breath samples which is generated by the orally ingested ^{13}C-urea. The treatment of the patient with antibiotics can cause false negative results[16].

- **Stool antigen test** has high sensitivity and high specificity. The method depends on the detection of the antibodies in the stool. False negatives can be obtained due to the treatment of the patient with antibiotics as proton pump inhibitors(PPI)[17].

- **Blood-based tests (serology)** depends on the diagnosis of the antibodies formed in response to an infection in the serum[15].

3. CriteriaTo Evaluate The Diagnosis Methods

Among the various tests, the choice of test should be based on some criteria, such as **sensitivity** and **specificity** of the test, the **cost**, the **prevalence** of the infection in the population; the **age**, **gender**, **signaling symptoms** and the **family history** of the patient, the **availability** of the tests as laboratory equipment and trained skills.

Sensitivity and **specificity** areknown as classification function in statistics[15]. **Sensitivity** is ameasure of the proportion of actual positives which are correctly identified. In statistics, type II error represents the "false negative rate" and it determines the sensitivity rate. Sensitivity is calculated as

$$Sensitivity = \frac{true\ positive}{true\ positive\ + false\ negative}$$

Specificity measures the proportion of negatives which are correctly identified. In statistics, type I error represents the "false positive rate" and it determines the specificity rate.

$$Specificity = \frac{true\ negative}{true\ negative\ + false\ positive}$$

The prevalence of the *H.pylori* in the population is effective on the obtaining positive and negative results. If the prevalence of the gastric diseases as cancer is high, invasive tests are better for primary diagnosis [12].

The diagnosis methods' specificity and sensitivity can be affected by the treatment of the patient with drugs as proton pump inhibitors (PPI),bismuth, etc. since the medicines can suppress the diagnosis and can give false negative results. Therefore the treatment needs to be stopped for a sufficient time interval (from 1 week to 4 week) depending on the dose and the duration of the treatment before testing[9].

The gastric symptoms observed in the family history of the patient and the signaling symptoms that affect the type of the diagnosis method. For the young patients with dyspepsia and without signaling symptoms noninvasive methods are suggested, but the patients older than 45 years and positive family history are suggested to be diagnosed with invasive methods[18].

The cost of the test change according to the country and the length of analysis for the test vary from 0.5 hour to 7 laboratory days[19].

4. Literature Review of the Diagnosis Methods

The diagnosis methods of *H. pylori* are classified as invasive and non-invasive and their attributes in terms of sensitivity, specificity, cost, easiness, time and effectiveness have distinct values from each other. The attributes of the tests are summarized in Table 1.

In the studies of Vaire et al. [20], 375 patients are considered in which 45.3% of them are H.pylori positive. The aim of the test was obtaining the sensitivity and specificity of rapid urease test(RUT). The values obtained for 1 min, 5 min and 60 min RUT are 90.3%, 94.5% 96.2% for sensitivity and 98%, 95.6%, 95.6% for specificity.

For histology, Lunet et al.[21] compared Portuguese and Mozambicanpatients. It is found that, among those classified as positive byPCR, sensitivity of histology was 96.2% in Portugal and 66.3% in Mozambique.

Marusić[22]investigated 276 patients with dyspeptic symptoms. The sensitivity and specificity of culture from biopsies are found as 90-95%and 100% respectively. Judith Weiss [23]has done a study on 95 patients and found sensitivity and specificity of culture from biopsies as 94% and 100% respectively.

PCR method has types as RAPD, RFLP and REP and Evans D.J. [24]and Weiss [23]found the sensitivity and specificity of PCR as greater than 95%.

5. Analytic Network Process

Analytic network process (ANP) is a decision making method [25]. Decision making needs analysis and break down of the problem into its constituent parts to study their effect on the hypothesis [26]. Decision making can be either traditional deductive method which starts with the assumptions and makes deductions derived from them. The alternative method is holistic approach in which all factors and criteria are considered in advance in a hierarchy or in a network to analyze the dependencies [27]. The factors and criteria effecting the decision making process can be physical (tangible) and psychological (intangible) events as subjective ideas, feelings, and beliefs[28].

ANP is a more general form of the analytic hierarchy process (AHP) which consists of a goal, criteria, and alternatives used in multi-criteria decision analysis [29].

ANP structures a decision problem as a network and does not require independence among elements in the hierarchy, i.e. goal, criteria and alternatives since in many real-world cases there is interdependence among the items[26].

ANP analyses the elements in the interactive environment by grouping them as benefits (B), opportunities (O), costs (C) and risks (R). The interdependencies of the elements in the interactive environment are quantified with the weights. ANP develops a supermatrix by considering these weights and lists the feedback relationship between the elements at different layers and interdependence between elements at the same layer (Figure 2) [28].

5.1. The Supermatrix

All priority matrices in the network can be combined into a “supermatrix”, in which each entry indicates the influence of the “row element i” on the “column element j” (W_{ij}) and each cluster contains its own elements (e_i) (Figure 1)[30].

	Diagnostic method	Types of method	Sensitivity	Specificity	Cost	Easiness	Time	Effectiveness in treatment
INVASIVE METHODS	**Rapid urease test**	(results in 1 , 5 , 60 min)	(90.3%[2] , 94.5%[2], 96.2%[2]), 90–95%[13], 88%[18],	98%[2,13],95.6%[2,18],	$6.77	NA	2 hours	Very convenient and highly accurate
	Histology		(96.2%[a], 66.3%[b])[3], 95%[13],	95%[13],	$40.29	Easy	1-2 laboratory day	can also be used to determine the morphological characteristics of gastritis[13],
	Culture from gastric biopsies		90–95%[13],70%[18],	100%[13],97.8%[18],	$29.08	Difficult for isolation, transportation, culture media	7 laboratory days	Allow the determination of strain resistance against antibiotics
	Molecular Methods	RAPD-PCR* RFLP-PCR** REP-PCR***	>95%[17], 94%[18],	>95%[17], 100%[18],	NA	NA	NA	NA
NON -INVASIVE METHODS	**Serology**		80% [7],	91%[7],	Low cost	Easy performance , useful in region with lower prevalence	0-1 laboratory day	Lower diagnostic accuracy and useable for screening H.pylori infection
		ELISA	94.9%[13],	80.1%[13],	$39			
		CFT	93.1%[13],	78.4%[13],	NA			
	Urea breath test	^{13}C	98%[4], 90.6%[10], 95–98%[13],	96%[4], 99.2%[10] , 95–98%[13],	$60[19]	Can be done 4 weeks of antimicrobial therapy completion, EASY, suitable for children	0.5 hour	Radioactive, high diagnostic accuracy pre and post treatment condition
		^{14}C	98%[14], 94%[15], 90%[16],90%[19]	100%[14], 89%[15], 96%[16],95%[19]	Expensive equipment[19]			
	Stool antigen tests (HpSA)	ELISA	97%[11] , 90% [12],	87%[11], 98% [12],	$90-95	Easy, suitable for children	1 laboratory day	high diagnostic accuracy pre and post treatment condition,
		RAPID HpStAR	86–91%[5], 88%[6], 91–92% [9],	91–93%[5], 98% [6], 76–80% [8],	NA			
		Amplified IDEIA HpStAR	95%[5] , 90%[8],	98%[5] , 89%[8],	NA			
		PCR	83.8% [8],	98.4%[8],	NA			

RAPD: Randomly Amplified Polymorphic DNA PCR, RFLP**: Restriction Fragment Length Polimorhism , REP***: Repetitive ExtragenicPalindormic , ELISA: Enzyme Linked ImmunoSorbant Assay.*

1 Calvet, X., Sánchez-Delgado, J., Montserrat, A., Lario, S., Ramírez-Lázaro, M.J., Quesada, M., Casalots, A., Suárez, D., Campo, R., Brullet, E., 2009. Accuracy of diagnostic tests for Helicobacter pylori: a reappraisal. Clinical Infectious Diseases 48, 1385–1391.
2 Vaira, D., Gatta, L., Ricci, C., Perna, F., Saracino, I., Fiorini, G., Castelli, V., Holton, J., 2010. A comparison amongst three rapid urease tests to diagnose Helicobacter pylori infection in 375 consecutive dyspeptic. Internal and emergency medicine 5, 41–47.
3 Lunet, N., Peleteiro, B., Carrilho, C., Figueiredo, C., Azevedo, A., 2009. Sensitivity is not an intrinsic property of a diagnostic test: empirical evidence from histological diagnosis of Helicobacter pylori infection. BMC gastroenterology 9, 98.
4 Elitsur, Y., Tolia, V., Gilger, M.A., Reeves-Garcia, J., Schmidt-Sommerfeld, E., Opekun, A.R., El-Zimaity, H., Graham, D.Y., Enmei, K., 2009. Urea breath test in children: the United States prospective, multicenter study. Helicobacter 14, 134–140.
5 Prell, C., Osterrieder, S., Lottspeich, C., Schwarzer, A., Rüssmann, H., Ossiander, G., Koletzko, S., 2009. Improved performance of a rapid office-based stool test for detection of Helicobacter pylori in children before and after therapy. Journal of clinical microbiology 47, 3980–3984.
6 Kalach, N., Benhamou, P.H., Raymond, J., Bergeret, M., Barbet, P., Briet, F., Flourié, B., Senouci, L., Gendrei, D., Dupont, C., 1995. A controlled study of the efficacy of lansoprazole in combination with two different dual antibiotic associations during Helicobacter pylori (H pylori) gastric infection in children. Gastroenterology 108, A1231.
7 Nguyen, L.T., Uchida, T., Tsukamoto, Y., Trinh, T.D., Ta, L., Ho, D.Q.D., Matsuhisa, T., Uchida, M., Takayama, A., Hijiya, N., 2010. Evaluation of rapid urine test for the detection of Helicobacter pylori infection in the Vietnamese population. Digestive diseases and sciences 55, 89–93.
8 Vécsei, A., Innerhofer, A., Binder, C., Gizci, H., Hammer, K., Bruckdorfer, A., Riedl, S., Gadner, H., Hirschl, A.M., Makristathis, A., 2010. Stool Polymerase Chain Reaction for< i> Helicobacter pylori</i> Detection and Clarithromycin Susceptibility Testing in Children. Clinical Gastroenterology and Hepatology 8, 309–312.
9 Calvet, X., Lehours, P., Lario, S., Mégraud, F., 2010. Diagnosis of Helicobacter pylori infection. Helicobacter 15, 7–13.
10 Vaira, D., Malfertheiner, P., Mégraud, F., Axon, A.T., Deltenre, M., Gasbarrini, G., O'Morain, C., Garcia, J.M.P., Quina, M., Tytgat, G.N., 2000. Noninvasive antigen-based assay for assessing Helicobacter pylori eradication: a European multicenter study. The American journal of gastroenterology 95, 925–929.
11 Ohkura, R., Miwa, H., Murai, T., Nagahara, A., Ohta, K., Sato, K., Yamada, T., Sato, N., 2000. Usefulness of a novel enzyme immunoassay for the detection of Helicobacter pylori in feces. Scandinavian journal of gastroenterology 35, 49–53.
12 Ishihara, S., Kaji, T., Kawamura, A., Rumi, M.A., Sato, H., Okuyama, T., Adachi, K., Fukuda, R., Watanabe, M., Hashimoto, T., 2000. Diagnostic accuracy of a new non-invasive enzyme immunoassay for detecting Helicobacter pylori in stools after eradication therapy. Alimentary Pharmacology and Therapeutics 14, 611–614.
13 Maru\vsić, M., Prese\vcki, V., Kati\vcić, M., Dominis, M., Kalenić, S., 2006. The place and role of serologic methods in detecting Helicobacter pylori infection. Collegium antropologicum 30, 529–533.
14 Desroches JJ. et al. 1997,
15 Debongie JC. et al. 1991,
16 Douglas et al.
17 Evans DG, 1995,
18 Weiss, J., Mecca, J., da Silva, E., Gassner, D., 1994. Comparison of PCR and other diagnostic techniques for detection of Helicobacter pylori infection in dyspeptic patients. Journal of clinical microbiology 32, 1663–1668.
19 Marshall, B.J., Surveyor, I., 1988. Carbon-14 urea breath test for the diagnosis of Campylobacter pylori associated gastritis. J Nucl Med 29, 11–16.

Table 1 : Comparison of Invasive and Noninvasive Methods

$$W=\begin{array}{c} \\ C_1 \\ \\ \\ C_2 \\ \\ \\ \vdots \\ \\ C_m \\ \\ \end{array}\begin{array}{c} \begin{array}{cccc} C_1 & C_2 & \cdots & C_m \\ e_1^1\ e_1^2 \ldots e_1^{n1} & e_2^1\ e_2^2 \ldots e_2^{n2} & & e_m^1\ e_m^2 \ldots e_m^{nm} \end{array} \\ \begin{bmatrix} W_{11} & W_{12} & \cdots & W_{1m} \\ W_{21} & W_{22} & \cdots & W_{2m} \\ \vdots & \vdots & \vdots & \vdots \\ W_{m1} & W_{m2} & \cdots & W_{mm} \end{bmatrix} \end{array}$$

Figure 1: Supermatrix in ANP

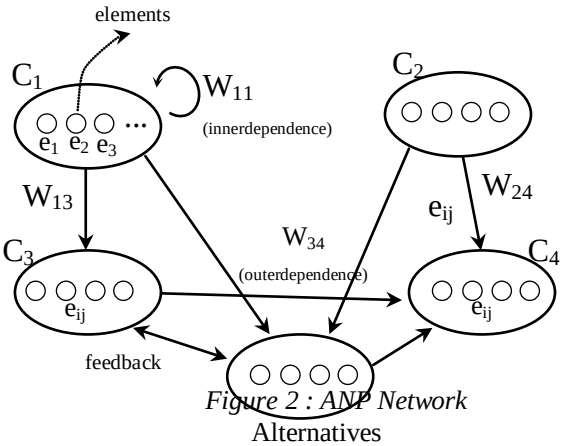

Figure 2 : ANP Network

The fundamental requirement for developing the supermatrix in the ANP is the control element for these pairwise comparisons that can be the element at the upper or lower layers of the network structure.

For the purpose of pairwise comparison, a scale of measure from 1 to 7 is developed, denoting indifferent to absolutely important, respectively. Reasonably, the reciprocal scale of measure from 1 to 1/7 will denote indifferent to absolutely unimportant, respectively[26].

The relative weights of importance is represented by the number $\mathbf{c_{ij}} = \mathbf{w_i/w_j}$ indicating the strength of behavior i when compared with behavior j will be derived from the subjective judgment of pairwise comparison. In the pairwise comparisons the diagonal of this comparison matrix C consists of ones. The relative weight vector must satisfy the equation **Cw = nw** provided that we can make a perfect comparison and create a **n**x**n** comparison matrix[25].

The comparison is made by subjective judgment. Based on the theory of matrix, the small variations of the comparison of c_{ij} will keep the largest **eigenvalue** close to **n**. Consequently, the relative vector of weight w is computed as the unique solution of $\mathbf{Cw=\lambda_{max}w}$ where C is the comparison matrix and $\mathbf{\lambda_{max}}$ is the largest eigenvalue of C. There are several algorithms available for approximating vector w[31].

There are three supermatrices associated with each network:

- **UnweightedSupermatrix**,
- **Weighted Supermatrix** and
- **Limit Supermatrix**[25].

In order to compute the final limit matrix, the supermatrix, which has been ensured of column

stochastic, has to raise to high power until weights have been converged and remain stable[25].

Based on the final limit matrix **alternatives can be ranked.**

The steps that must be followed during the solution of problem with ANP can be summarized as follows.

Steps of ANP [31]

- **Understand** the decision problem in detail, including its **objectives**, **criteria** and **sub criteria**, **actors** and their **objectives** and the **possible outcomes** of that decision.
- **Determine** control criteria and sub criteria in the four control hierarchies' one each for the benefits, opportunities, costs and risks of that decision and obtain their priorities from paired comparison matrices.
- **Determine** a complete set of network clusters (components) and their elements that are relevant to each and every control criterion.
- For each control criterion or sub-criterion, determine the appropriate subset of clusters of the comprehensive set with their elements and connect them according to their outer and inner dependence influences.
- Determine cluster or elements influencing or being influenced by other clusters and elements.
- Perform **sensitivity analysis** on the final outcome to see if the final answer is stable to changes in the inputs.

6. The application of the ANP

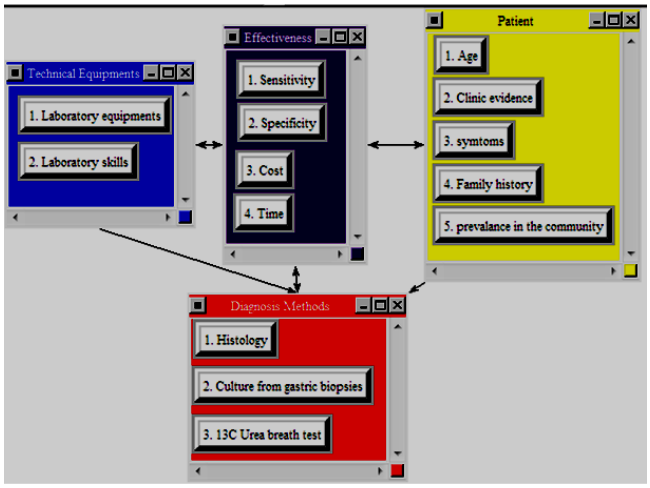

Figure 3.ANP structure in Superdecisions program

Sensitivity , specificity, cost and **time** of the test, the **age, gender, signaling symptoms** and **family history** of the patient and the **prevalence** of the infection in the population, the **availability** of the tests as **laboratoryequipment** and **trained skills** are the criteria to select the diagnosis method of H.pylori.

The weight of the test effectiveness criteria are based on the diagnosis methods' attributes of the patient and the technical equipment's. The alternatives that are compared in this study histology, culture from gastric biopsies, 13C urea breath test have almost the same sensitivity and specificity values (Table 1), therefore the weight of these criteria are altered.

7. Conclusion

Helicobacter pylori is a bacteria causing *gastroduodenal* diseases. The diagnosis of the bacteria is vital for the treatment and prevent ulcer and gastric cancer. The diagnosis methods are classified as invasive and noninvasive and in each group there are tests as rapid urease test, histology, culture from gastric biopsies, molecular methods, serology, urea breath test and stool antigen tests (HpSA).

The methods are differentiated from each other according to their sensitivity, specificity values in the literature. There are also other criteria as cost,easiness, time to get result for the tests and also there are criteria related to the patients as age, clinic evidences symptoms, family history and prevalence in the community.

For the diagnosis methods, three commonly used alternatives histology, culture and carbon-13 urea breath test are selected and compared with ANP according to the mentioned criteria.

In the limit matrix obtained from Superdecisionsprogram, carbon-13 method is ranked in the first place according to the weights of the criteria, then it comes culture and histology (Table 2).

Table 2.The limit matrix values for diagnosis methods.

Criteria	Weights
1. C-13 urea breath test	0.10380
2. Culture	0.09104
3. Histology	0.09087

The attributes of the diagnosis methods are compared and according to the results specificity has the highest rank, then it comes sensitivity, cost and time. The reason that specificity is highest is due to

the importance of the diagnosis of the true negatives.(Table 3)

Table 3. The limit matrix values for criteria

Criteria	Weights
1.Specificity	0.16367
2.Sensitivity	0.13612
3. Cost	0.07371
4. Time	0.05507

In selection of the diagnosis methods, the patients age, clinical evidence, symptoms, family background and prevalence of the H. pylori in the population that the patient is living are factors that should be considered. Among these factors, the most important is found as clinical evidences, then symptoms, age, family background and prevalence (Table 4)

Table 4. The limit matrix values for patients' properties

Criteria	Weights
1. Clinical evidences	0.06969
2. Symptoms	0.03867
3. Family background	0.01933
4. Prevalence	0.00967
5. Age	0.00551

Diagnosis is vital for the treatment and prevention of the bacteria related illnesses. The alternatives given in this study can be expanded in future studies and more criteria can be added to the model to find out which methods are efficient for a certain combination of criteria and attributes of the patients.

References

[1].Classen, M., Prinz, C., You, W., 2010. Helicobacter pylori: a bacterium that can lead to cancer of the stomach. Strict. Embargoed Publ. 00 01am Est 28th January 2010 35.

[2]. Weyermann, M., Rothenbacher, D., Brenner, H., 2009. Acquisition of Helicobacter pylori infection in early childhood: independent contributions of infected mothers, fathers, and siblings. Am. J. Gastroenterol. 104, 182–189.

[3]. Atherton, J.C., Cao, P., Peek, R.M., Tummuru, M.K., Blaser, M.J., Cover, T.L., 1995. Mosaicism in vacuolating cytotoxin alleles of Helicobacter pylori association of specific vacA types with cytotoxin production and peptic ulceration. J. Biol. Chem. 270, 17771–17777.

[4]. Brown, L.M., 2000. Helicobacter pylori: epidemiology and routes of transmission. Epidemiol. Rev. 22, 283.

[5]. Bytzer, P., Dahlerup, J.F., Eriksen, J.R., Jarbøl, D., Rosenstock, S., Wildt, S., 2011. Diagnosis and treatment of Helicobacter pylori in-fection. Dan Med Bull 58, C4271.

[6]. Vakil, N., Rhew, D., Soll, A., Ofman, J.J., 2000. The cost-effectiveness of diagnostic testing strategies for Helicobacter pylori. Am. J. Gastroenterol. 95, 1691–1698.

[7]. Campbell, M.J., Machin, D., 1993. Medical statistics: a commonsense approach. Wiley London.

[8].Ndip, R.N., Malange Tarkang, A.E., Mbullah, S.M., Luma, H.N., Malongue, A., Ndip, L.M., Nyongbela, K., Wirmum, C., Efange, S., 2007. < i> In vitro</i> anti-< i> Helicobacter pylori</i> activity of extracts of selected medicinal plants from North West Cameroon. J. Ethnopharmacol. 114, 452–457.

[9]. Hunt, R.H., Xiao, S.D., Megraud, F., Leon-Barua, R., Bazzoli, F., Van Der Merwe, S., Vaz Coelho, L.G., Fock, M., Fedail, S., Cohen, H., 2011. Helicobacter pylori in developing countries. World Gastroenterology Organisation Global Guideline. J Gastrointestin Liver Dis 20, 299–304.

[10].Vécsei, A., Innerhofer, A., Graf, U., Binder, C., Giczi, H., Hammer, K., Bruckdorfer, A., Hirschl, A.M., Makristathis, A., 2011. Helicobacter pylori eradication rates in children upon susceptibility testing based on noninvasive stool polymerase chain reaction versus gastric tissue culture. J. Pediatr. Gastroenterol. Nutr. 53, 65–70.

[11].Tang, J.-H., Liu, N.-J., Cheng, H.-T., Lee, C.-S., Chu, Y.-Y., Sung, K.-F., Lin, C.-H., Tsou, Y.-K., Lien, J.-M., Cheng, C.-L., 2009. Endoscopic diagnosis of Helicobacter pylori infection by rapid urease test in bleeding peptic ulcers: a prospective case-control study. J. Clin. Gastroenterol. 43, 133–139.

[12].Leodolter, A., Wolle, K., Malfertheiner, P., 2001. Current standards in the diagnosis of Helicobacter pylori infection. Dig. Dis. 19, 116–122.

[13]. Guarner, J., Kalach, N., Elitsur, Y., Koletzko, S., 2010. Helicobacter pylori diagnostic tests in children: review of the literature from 1999 to 2009. Eur. J. Pediatr. 169, 15–25.

[14].Babić, T., Miljković-Selimović, B., Kocić, B., Nagorni, A., Ristić, L., 2012. Successful isolation of Helicobacter pylori after prolonged incubation: A case report of prolonged

incubation for H. pylori. Arch. Biol. Sci. 64, 1297–1299.

[15]. Calvet, X., Lehours, P., Lario, S., Mégraud, F., 2010a. Diagnosis of Helicobacter pylori Infection. Helicobacter 15, 7–13.

[16].Velayos, B., Fernández-Salazar, L., Pons-Renedo, F., Muñoz, M.F., Almaraz, A., Aller, R., Ruíz, L., Del Olmo, L., Gisbert, J.P., González-Hernández, J.M., 2012. Accuracy of urea breath test performed immediately after emergency endoscopy in peptic ulcer bleeding. Dig. Dis. Sci. 57, 1880–1886.

[17]. Raguza, D., Machado, R.S., Ogata, S.K., Granato, C.F.H., Patrício, F.R.S., Kawakami, E., 2010. Validation of a monoclonal stool antigen test for diagnosing Helicobacter pylori infection in young children. J. Pediatr. Gastroenterol. Nutr. 50, 400–403.

[18]. Han, M.A., Oh, M.G., Choi, I.J., Park, S.R., Ryu, K.W., Nam, B.-H., Cho, S.-J., Kim, C.G., Lee, J.H., Kim, Y.-W., 2012. Association of family history with cancer recurrence and survival in patients with gastric cancer. J. Clin. Oncol. 30, 701–708.

[19]. Holmes, K.P., Fang, J.C., Jackson, B.R., 2010. Cost-effectiveness of six strategies for Helicobacter pylori diagnosis and management in uninvestigated dyspepsia assuming a high resource intensity practice pattern. BMC Health Serv. Res. 10, 344.

[20].Vaira, D., Malfertheiner, P., Mégraud, F., Axon, A.T., Deltenre, M., Gasbarrini, G., O'Morain, C., Garcia, J.M.P., Quina, M., Tytgat, G.N., 2000. Noninvasive antigen-based assay for assessing Helicobacter pylori eradication: a European multicenter study. Am. J. Gastroenterol. 95, 925–929.

[21].Lunet, N., Peleteiro, B., Carrilho, C., Figueiredo, C., Azevedo, A., 2009. Sensitivity is not an intrinsic property of a diagnostic test: empirical evidence from histological diagnosis of Helicobacter pylori infection. Bmc Gastroenterol. 9, 98.

[22].Marusić, M., Presecki, V., Katić, M., Dominis, M., Kalenić, S., 2006. The place and role of serologic methods in detecting Helicobacter pylori infection. Coll. Antropol. 30, 529–533.

[23].Weiss, J., Mecca, J., da Silva, E., Gassner, D., 1994. Comparison of PCR and other diagnostic techniques for detection of Helicobacter pylori infection in dyspeptic patients. J. Clin. Microbiol. 32, 1663–1668.

[24]. Evans, D.J., Evans, D.G., Takemura, T., Nakano, H., Lampert, H.C., Graham, D.Y., Granger, D.N., Kvietys, P.R., 1995. Characterization of a Helicobacter pylori neutrophil-activating protein. Infect. Immun. 63, 2213–2220.

[25]. Saaty, T.L., 2004. Fundamentals of the analytic network process—Dependence and feedback in decision-making with a single network. J. Syst. Sci. Syst. Eng. 13, 129–157.

[26]. Saaty, T.L., Shih, H.-S., 2009. Structures in decision making: On the subjective geometry of hierarchies and networks. Eur. J. Oper. Res. 199, 867–872.

[27].Balnaves, M., Caputi, P., 2001. Introduction to quantitative research methods: An investigative approach. SAGE Publications Limited.

[28].Saaty, T.L., Begicevic, N., 2012. The analytic hierarchy process applied to complexity. Int. J. Econ. Bus. Res. 4, 266–283.

[29].Sipahi, S., Timor, M., 2010. The analytic hierarchy process and analytic network process: an overview of applications. Manag. Decis. 48, 775–808.

[30]. Tsai, W.-H., Chou, W.-C., 2009. Selecting management systems for sustainable development in SMEs: A novel hybrid model based on DEMATEL, ANP, and ZOGP. Expert Syst. Appl. 36, 1444–1458.

[31].Saaty, T.L., Vargas, L.G., 2006. Decision making with the analytic network process: economic, political, social and technological applications with benefits, opportunities, costs and risks. Springer Science+ Business Media.