Prevalence of Helicobacter Pylori Infection in a Sample of Egyptian Patients with Type 2 Diabetes Mellitus

Ihab M. Salem, Khaled M. Hadhoud , A.F. Zeid and Nagwa M. Shawky*
Departments of Internal Medicine and Clinical Pathology*,

Abstract

Background: Some studies have shown *Helicobacter pylori* (*H. pylori*) infection to be associated with diabetes mellitus, but this relationship remains controversial.

Objective: This study was planned to determine the prevalence of *H. pylori* in Egyptian patients with type 2 diabetes mellitus (type 2DM) and to evaluate the relationship between *H. pylori* and glycemic control and to find out a possible relation of *H. pylori* to various diabetic complications.

Subjects & Methods: The study included 80 patients which were divided into 2 main groups: Group I included 60 type 2 diabetic patients and further subdivided in to 2 subgroups according to the r presence of complications either macro – or microvascular. (Group 1a, Group 1b) respectively, each of the subgroups comprised 30 patients. Group II included 20 healthy subjects as control group. All patients were subjected to thorough clinical examination and investigations that included CBC, lipid profile, HbAlc, fasting & 2 HPP blood glucose, urine examination for microalbuminuria, fundus examination of retinopathy, ECG, CT or MRI brain in addition to *H. pylori* stool antigen: ***Results:***. thirty four (56.7%) diabetic patients were + ve for H. pylori infection compared to controls in which 6 subjects (30%) were positive (p= 0.039). Diabetic patients with complications had higher frequency of H. pylori infection when compared to patients without complications (X = ,p = 0.037). But, non significant differences were detected between patients with macro- and microvascular complications regarding H. pylori infection (p = 0.69). Infected patients with H. pylori had significantly higher HbAlc, cholesterol & triglycerides (TG) levels than non infected (p = 0.001, 0.002, 0.031, respectively). Also, in complicated diabetic patients, infected cases had significantly higher HbA1c, cholesterol and TG levels than non infected (p= 0.007, 0.008, 0.022, respectively). Finally , infected cases with H. pylori in complicated diabetic patients had significantly longer disease duration and higher Body Mass Index (BMI) values than non infected (p = 0.0001, 0.007, respectively). ***Conclusion:*** *H. pylori* infection is more prevalent in diabetic patients especially complicated cases and *H. pylori* infection is related to poor glycemic control ,long duration of diabetes and overweight. It is recommended to test for and eradicate *H. pylori* infection, if present, in diabetics to achieve better glycemic control or even to reduce serious complications.

Keywords: *Helicobacter pylori*, type 2 DM.

INTRODUCTION

*Helicobacter pyl*ori is a Gram-negative, microaerophilic bacterium that can inhabit various areas of the stomach particularly the antrum. It is acquired usually before the age of 10 and is transmitted mainly in families and the most common route of infection is either oral to oral or fecal to oral contact[(1)]. Over 80% of individuals infected with the bacterium are asymptomatic[(2)]. It causes a chronic low-level inflammation of the stomach lining and is strongly linked to the development of duodenal and gastric ulcers. Also, previous studies had confirmed the bacterium's link to stomach cancer and elucidated genes associated with its virulence, particularly a gene called cytotoxic associated gene[Cag A][(1,2)].

More than 50% of the world's population harbor *H. pylori* in their upper gastrointestinal tract. Infection is more prevalent in developing countries, and incidence is decreasing in Western countries[(3)].

It is a common infection in diabetic patients who have inadequate metabolic control as such individuals are colonized by *H. pylori* infection in the gastric antrum, probably because of

© 2014 British Journals ISSN 2047-3745

chemotactic factors such as tumor necrosis factor (TNF), Interleukins – IL_1, II_2, and IL_8 are present in gastric epithelium. These cytokines induce a number of changes in the gastric epithelium that promote inflammation and epithelial damage thus leading to increased risk of aberrant repair giving the picture of gastric atrophy or epithelial cell metaplasia[4].

Diabetes mellitus is one of the important causes of dyspepsia. Beside DM the *H. pylori* is also a well established cause of dyspepsia. The incidence of *Helicobacter pylori* is increased in diabetes mellitus[5]. Delayed gastric emptying and antral dysmotility are important causes of dyspepsia in diabetes. The role of *Helicobacter pylori* infection in diabetic dyspepsia is mainly related to blood glucose concentration. Hyperglycemia may induce the infection by *H. pylori* or the silent infection may get reactivated and produce symptoms of dyspepsia in diabetes[5].

Helicobacter pylori, may have an impact on cardiovascular conditions and metabolic syndrome[6-8] potentially mediated by elevations in inflammatory markers such as C-reactive protein (CRP) and interleukin (IL) -6[5]. Inflammation and activated innate immunity have also been implicated in the pathogenesis of diabetes through insulin resistance[9]. For example, elevated levels of inflammatory cytokines may lead to phosphorylation of serine residues on the insulin receptor substrate, which prevents its interaction with insulin receptors, inhibiting insulin action[9]. Lipopolysaccharides from pathogens in the gut have also been linked to the activation of toll-like receptors, resulting in energy harvesting, fat accumulation and stimulation of the innate immune system, and consequent insulin resistance[10]. However, epidemiological studies investigating the impact of pathogen burden on diabetes have been limited [11].

Some studies have shown *Helicobacter pylori* (*H. pylori*) infection to be associated with diabetes, but the relationship remains controversial [12]. However, data on the prevalence of H. pylori in type 2 diabetes mellitus(T2 DM) patients are scarce and contradictory [13, 14]

Both the natural history of gastrointestinal symptoms and factors influencing symptom turnover in diabetes mellitus are unknown[15]. .

So this study was planned to determine prevalence of *H. pylori* in Egyptian patients with T2DM and to evaluate the relationship between *H. pylori* and glycemic control, also to find out a possible relation of *H. pylori* to various diabetic complications.

SUBJECTS AND METHODS

This study was carried out in the department of Internal Medicine, Endocrinology Unit, Faculty of Medicine, Zagazig University, Egypt, in the period between Sep.2012 to Sep.2013.

The study was conducted on 80 subjects. They were divided into 2 main groups:

Group I: It included 60 type 2 diabetic patients, 28 males and 32 females. The duration of diabetes was between 6-20 years with a mean value ± SD of (11.5 ± 3.6), their ages ranged between 40 – 59 years with a mean value ± SD of (49.3 ± 4.14). This group was further subdivided into 2 subgroups according to absence or presence of, either macrovascular or microvascular complications [Group Ia = 30 patients,. Group Ib = 30 patients respectively]

Group II (control group): It comprised 20 healthy subjects, 9 males, 11 females matched for age and sex as diabetic group (mean age 46.7 ± 5.3).

Patients were randomly selected from those attending the diabetes outpatient clinic of Zagazig University Hospitals ***After being informed on the purpose and procedures of the study, all subjects signed an informed consent form.***

Patient were excluded from the study if they were diagnosed previously to have *H. pylori* infection or those who had undergone or were currently undergoing *H. pylori* eradication. Also those receiving anti-ulcer treatment in the last 3 months or still receiving proton pump inhibitors (PPI) or H_2 receptor blocker. Also, we excluded type 1 diabetics and non–cooperative patients from this study.

All patients and control subjects were submitted to full clinical assessment including history taking & thorough clinical examination including Body Mass Index (BMI) and waist

circumference in addition to the following investigations:

*Routine laboratory investigations including HbAlc, lipid profile and CBC, fasting & 2H blood glucose [FBG, 2 HPPBG], blood urea, S. creatinine & LFT.

*Urine examination for microalbuminuria "for diagnosis of nephropathy", (expressed as microalbumin/creatinine as Alb/Cr ration in untimed random sample correlate well with 24h excretion) according to **Ritzmann and Daniels** [16].

*Fundus examination of eyes for diagnosis of retinopathy.

*Color doppler examination of peripheral arteries in patients with history of intermittent claudication. Peripheral vascular disease (PVD) was defined as an ankle brachial index of 0.8 or less [17].

*ECG to document angina or myocardial infarction [especially in subjects with self reported and confirmed history of coronary artery disease "CAD"][18].

*CT scan on the brain or MRI to diagnose stroke, which was defined as a clinical syndrome consisting of neurological findings persisting > 24 hours with documented radiological finding [19].

******Helicobacter pylori* **stool antigen detection:**

Method:

This enzyme immunoassay employs a mixture of monoclonal anti-*H. pylori* antibodies as capture antibody and a mixture of peroxidase-conjugated monoclonal anti-*H. pylori* antibodies as detection antibody. Based on the intensity of color developed, results are reported as *H. pylori* antigen detected, not detected or indeterminate.

Performance characteristics have not been established for watery diarrheal stools or for asymptomatic individuals.

Interpretive Information:

A positive result (antigen detected) is indicative of *H. pylori* presence. A negative result (antigen not detected) indicates absence of *H. pylori* or an antigenic level below the assay limit of detection. The test has a sensitivity and specificity of 96% for detecting *H. pylori* infection. False-negative results may be obtained on specimens from patients who have ingested selected medications (antimicrobials, proton pump inhibitors, bismuth preparations) within the 2 weeks prior to specimen collection. If clinically indicated, the test may be repeated on a new specimen obtained 2 weeks after stopping treatment with these medications. Positive results are not affected by medication.

A positive result ≥ 7 days after starting therapy is indicative of ineffective treatment or recurrence. Testing for eradication should be performed ≥ 4 weeks post therapy; a negative result at this time indicates eradication of the infection. Intermediate results require retesting with a new specimen [20].

Statistical analysis:

Data obtained from the present study were computed using SPSS versions 17 under the platform of Microsoft Windows XP, Professional Edition. Continuous data were expressed in the form of mean ± SD while categorical data were expressed in the form of count and percent. Comparison of continuous data were performed utilizing Student t test, while categorical data were done using Chi-square test. P value less than 0.05 was considered statistically significant.

RESULTS

Table (1): Comparison between patients and controls regarding the prevalence of *H. pylori* infection:

		Patients (n=60)	***Controls (n=20)***	***Chi-square test***	
				X2	***P***
H. pylori	+ve	34 (56.7 %)	6 (30.0 %)	4.3	0.039*
	-ve	26(43.3%)	14 (70.0%)		

© 2014 British Journals ISSN 2047-3745

* = p is significant

It shows higher frequency of *H. pylori* infection in diabetic patients when compared with controls.

Table (2): Comparison between complicated and uncomplicated diabetic patients regarding the prevalence of *H. pylori* infection:

		Patients with complications (n=30)	***Patients without complications (n=30)***	***Chi-square test***	
				X^2	***P***
H. pylori	+ve	20 (66.7 %)	14 (46.7 %)	4.3	0.037*
	-ve	10 (33.3%)	16 (53.3%)		

This table shows that patients with complications had higher frequency of *H. pylori* infection when compared with patients without.

Table (3): Comparison between patients with macrovascular and microvascular complications regarding the prevalence of *H. pylori* infection:

		Patients with macrovascular complications (n = 15)	**Patients with microvascular complications (n =15)**	**Chi-square test**	
				X^2	**P**
H. pylori	+ve	10(66.7%)	10(66.7%)	0.16	0.69
	-ve	5 (33.3 %)	5 (33.3 %)		

This table shows no statistically significant differences between patients with macrovascular and microvascular complications regarding the prevalence of *H. pylori*.

Table (4): Comparison between patients with and without *H.* pylori infection in diabetic patients regarding the laboratory findings:

	***H. pylori* +ve (n=34)**	***H. pylori* -ve (n-26)**	**Student t test**	
			t	**P**
WBCs / cmm	6.6 ± 2.0	6.9 ±2.1	-0.6	0.54
Platelets / cmm	246.7 ± 55.6	253.2 ±60.0	-0.4	0.66
Hb g/dl	13.4 ± 1.3	12.6 ±1.0	2.4	0.017
FBG mg/dl	195.4 ± 47.4	200.9 ±35.6	-0.49	0.62
2HPPBG mg/dl	336.2 ± 71.0	3 12.4 ±76.8	1.2	0.22
HbAlc %	8.0 ± 1.3	6.5 ±1.1	3.7	0.0001
Microalbuminuria mg/dl	30.6 ± 3 1.9	21. 8 ±24.0	1.16	0.24
Cholesterol mg/dl	220.5 ± 44.5	171.2 ±24.4	3.24	0.002

Triglycerides mg/dl	128. 8 ± 24.0	112.8 ±20.6	2.2	0.031
HDL mg/dl	69.0 ± 5 1.8	56.7 ±29.2	1.15	0.25
LDL mg/dl	91.4 ± 35.8	90.2 ±27.7	0.13	0.88

This table shows that infected patients had significantly higher HbAlc, cholesterol and triglycerides levels

Table (5): Comparison between patients with without *H. pylori* infection and in uncomplicated diabetic patients regarding the laboratory findings:

	***H. pylori* +ve (n=14)**	***H. pylori* -ve (n-16)**	**Student t test**	
			t	**P**
WBCs /cmm	7.6 ± 2.4	7.6 ± 2.3	0.03	0.97
Platelet /cmm	278. 7 ± 52.9	279.0 ± 59.3	-0.01	0.99
Hb g/dl	13.6 ±1.6	12.4 ± 1.0	2.3	0.025
FBG mg/dl	176.8 ± 27.6	199.3 ± 29.9	-2.1	0.04
2HPPBG mg/dl	3 18.0 ± 60.0	313.5 ± 77.1	0.17	0.86
HbAlc %	7.1 ± 1.1	6.4 ± 1.0	1.8	0.08
Microalbuminuria mg/dl	13.3 ± 3.4	14.0 ± 2. 7	-0.66	0.51
Cholesterol mg/dl	165.7 ± 17.8	163. 7 ± 16.1	0.31	0.75
Triglycerides mg/dl	116.4 ±13.8	115.6 ± 20.1	0.12	0.9
HDL mg/dl	41.9 ± 8.9	45.9 ± 9.8	-1.1	0.25
LDL mg/dl	107.8 ± 20.3	103.2 ±16.5	0.67	0.5

No statistically significant differences was detected.

Table (6): Comparison between patients *with without H. pylori* infection and in complicated diabetic patients regarding the demographic and clinical characteristics:

		H. pylori + ve (n=20)	***H, pylori – ve (n-10)***	***Student t test***	
				t	***P***
Age		51.7 ± 4.5	48.8 ± 4.4	1.68	0.1
BMI		35.3 ± 2.4	30.7 ± 1.6	2.86	0.007*
Disease duration		11.9 ± 3.0	9.5 ± 1.5	5.2	0.0001*
				Chi-square	
				X2	***P***
Sex	***Male***	13	5	0.63	0.43
	Female	7	5		

Patients with *H. pylori* infection had significantly longer disease duration and higher BMI values.

© 2014 British Journals ISSN 2047-3745

Table (7): Comparison between patients with without *H. pylori* infection in complicated diabetic patients regarding the laboratory findings:

	***H. pylori* +ve (n=20)**	***H. pylori* -ve (n-10)**	**Student t test**	
			t	**P**
WBCs /cmm	5.9 ± 1.3	5.9 ± 1.1	0.04	0.96
Platelets / cmm	224.3 ± 46.7	212.1 ± 32.7	0.73	0.46
Hb g/dl	13.3 ± 1.1	13.0 ±0.86	0.71	0.48
FBG mg/dl	208.4 ± 54.3	203.6 ± 44.9	0.24	0.8
2 HPPBG mg/dl	348.9 ± 76.7	310.7 ± 80.5	1.2	0.2
HbAlc %	8.14 ± 1.4	6.5 ± 1.3	2.8	0.007*
Microalbuminuria mg/dl	42.8 ± 37.1	34.4 ± 36.1	0.58	0.56
Cholesterol mg/dl	224.8 ± 41.3	183.2 ± 31.0	2.8	0.008*
Triglycerides mg/dl	132.4 ± 27.5	108.4 ± 21.5	2.4	0.022*
HDL mg/dl	88.0 ± 60.7	74.1 ± 40.9	0.65	0.52
LDL mg/dl	80.0 ± 40.2	69.4 ± 30.0	0.73	0.47

This table shows that infected patients had significantly higher HbAlc, cholesterol and triglycerides levels.

DISCUSSION

Since the discovery of *Helicobacter pylori*, it has been shown to have a world-wide distribution. It has been estimated that up to half of the world's population harbor the infection in their stomachs[21].

An increased prevalence of *H. pylori* infection among diabetes mellitus patients was first suggested by many reports. One of them, documented a *H. pylori* prevalence rate of 74.4% in Type 2 diabetes mellitus patients as against 50% in non-diabetic controls[22].

A large Australian study showed that there was no significant difference in prevalence of *H. pylori* infection in DM versus non-DM patients[23].

In the past few years, there has been increasing evidence that some atherogenic vascular risk factors (e.g., homeostatic factors and lipids) are liable to be altered by inflammation and infection by certain microbial agents including *Helicobacter pylori*[24].

Inflammation, immune mediated vascular damage, direct bacterial invasion of atherosclerosis plaques, and hyperhomocysteinemia are among the mechanisms contributing to atherogenic risk attributed to *H. pylori* [25].

Furthermore, DM is a major risk factor for atherosclerosis and its related cardiovascular and cerebrovascular diseases. Although DM is considered as a risk for developing many infections because of impaired immune status, the seroprevalence risk of *H. pylori* infection among patients with diabetes is still controversial [26].

So, the present study aimed to determine prevalence of *H. pylori* in patient with type 2

© 2014 British Journals ISSN 2047-3745

diabetes and to evaluate the relationship between *H. pylori* and glycemic control. Also, we aimed to find out the relation of H. pylori to various diabetic complications.

In the present study, it was found that 34 patients (56.7%) had +ve *H. pylori* infection compared to 6 control (30.0%) with a statistically significant difference between both groups (p = 0.039) [Table1]. This is in agreement with findings of ***Bener et al.,***[4] who aimed to determine the association between *Helicobacter pylori* infection and type 2 diabetes mellitus in the United Arab Emirates population. There was higher prevalence of *H. pylori* infection in diabetic obese patients than the non-diabetic subjects (23.6% vs 11.8%, p <0.001).

In addition, **Hamed et al**,[24] found a higher prevalence of *H. pylori* infection in Egyptian DM patients as compared to healthy controls.

Also, **Devrajani et al**,[27]found a statistically significant higher frequency of *H. pylori* infection in diabetic patients when compared with controls and concluded that diabetic patients are more prone and at risk to acquire *H. pylori* infection.

In our study, comparison between diabetic patients with complications and without complications regarding the prevalence of *H. pylori* infection had shown that patients with complications had higher frequency of *H. pylori* infection when compared with patients without [Table 2]. This is in agreement with ***Ohnishi et al,***[28] who examined the relationship between seropositivity of antibodies to *H. pylori* and arterial stiffness. They found that *H. pylori* infection is associated with arterial stiffness in patients with type 2 diabetes mellitus.

As regards to relationship between H. pylori and macro- and microvascular complication o diabetes , this study reported no significant difference between both groups regarding H. pylori prevalence[table 4] . this against the results reported by Hamed et al(24) who studied the association between diabetic vascular complications and H. pylori infection; and influence of H. pylori infection on atherosclerosis and inflammatory biomarkers, and they concluded that H. pylori infection is common in DM and seems to be linked to the presence of atherosclerosis and ischemic cerebrovascular stroke.

As regards to laboratory finding , our results reported a statistically significant higher HbA1c, cholesterol & TG levels in patients with +ve H. pylori infection in comparison with those without . These results were highly increased in complicated diabetic patients with +ve H. pylori infection compared to –ve case [Tables 5, 7]. This is in harmony with the study of **Fernandini-Paredes et al.,**[29] who evaluated the relationship between glycosylated hemoglobin (HbAlc) levels and *H. pylori* infection in a cohort of patients with type 2 diabetes mellitus. In this study, in spite of the fact that there was no statistically significant differences between patients with +ve and –ve *H. pylori* and glycemic control, HbAlc levels were significantly higher in patients with infection.

In harmony with our results are that of study done on Chinese population[30] and concluded that long-term *H. pylori* infection is significantly associated with high levels of HbAlc and decreased insulin secretion in this Chinese population. Proper screening for *H. pylori* infection combined with regular monitoring of blood glucose and HbAlc levels might be effective for the early detection of glucose dysregulation and prevention of type 2 diabetes. Also, others mentioned that *H. pylori* may affect the levels of two stomach hormones that help to regulate blood glucose and they suggest that eradication of *H. pylori* using antibiotics could be beneficial in decreasing elevated HbAlc[1].

In the present study comparison between patients with *H. pylori* infection and patients without in diabetic patients regarding the demographic and clinical characteristics had shown that patients with *H. pylori* infection had significantly longer disease duration and higher BMI values "especially in complicated cases" [Table 6]. This interesting finding is supported by the study of **Shin et al.,**[31] who aimed to evaluate the association between metabolic syndrome and *Helicobacter pylori* (HP) infection. This study confirmed a strong association between *H. pylori* infection and

metabolic syndrome and its components including obesity, hypertension and dyslipidemia. Interestingly, this was also true in patients with vascular complications but not in patients without reflecting the influence of the association between metabolic syndrome and its components and vascular complications in DM patients with *H. pylori* infection. In the same direction, it was hypothesized that having both high BMI and the presence of *H. pylori* infection would have synergistic effect, increasing HbAlc even more that the sum of the individual effect of either risk factor alone[(32)].

Conclusion & Recommendation:

We can conclude that *H. pylori* is more prevalent in diabetic patients especially complicated cases, either with macro- or microcvascular complications, and that *H. pylori* infection is related to poor glycemic control and overweight in diabetic patients.

. Further studies on the relationship between H. pylori& type 2- DM are necessary on a large number of patients

Lastely , we can conclude that, it may be beneficial for individuals at risk for diabetes to be tested for the presence of H. pylori infection & its proper treatment & eradication may be important for proper glycemic control or even reducing serious complications.

.

REFERENCES

1- Yu Chen and Martin J. Blaser: Association Between gastric *Helicobacter pylori* colonization and HbAlc level. Journal of Infectious Disease. DOI: 10.1093/ inFdis/ Jis 106, 2012.

2- Boyanova, L (editor): *Helicobacter pylori* casiter Academic Press 2011.

3- Brown LM: *Helicobacter pylori*; epidemiology and routes of transmission; Epidemiol Rev. 22 (2): 283 – 970, 2000.

4- Bener A, Micallef R, Afifl M, Derbala M, Al-Mulla HM, Usmani MA: Association between type 2 diabetes mellitus and *Helicobacter pylori* infection. Turk J Gastroenterol. 18 : 225 – 9, 2007.

5- Saluja JS, Ajinkya M, Khemani B, Khanna S, Jain R: *Helicobacter pylori* and diabetes mellitus. Bombay Hosp J. 44: 57 – 60, 2002.

6. Georges JL, Rupprecht HJ, Blankenberg S, et al.: Impact of pathogen burden in patients with coronary artery disease in relation to systemic inflammation and variation in genes encoding cytokines. Am J Cardiol, 92: 515 – 521, 2003.

7- Simanek AM, Dowel JB, Aiello AE: Persistent pathogens linking socioeconomic position and cardiovascular disease in the US. Int J Epidemiol, 38: 775 – 787, 2009.

8- Nabipour I, Vahdat K, Jafari SM, Pazoki R, Sanjdideh Z: The association of metabolic syndrome and *Chlamydia pneumoniae*, *Helicobacter pylori*, cytomegalovirus, and herpes simplex virus type 1: the Persian Gulf Healthy Heart Study. Cardiovasc Diabetol, 5: 25, 2006.

9- Wellen KE, Hotamisligil GS: Inflammation, stress, and diabetes. J Clin Invest, 115: 1111 – 1119, 2005.

10- Manco M, Putignani I, Bottazzo GF: Gut microbiota, lipopolysaccharides, and innate immunity in the pathogenesis of obesity and cardiovascular risk. Endocr Rev, 31: 817 – 844, 2010.

11- Christie Y. Jeon, Mary N. Haan, Caroline Cheng et al.,: *H. pylori* is associated with an increased risk of diabetes. Diabetes Care, 35: 520 – 25, 2012.

12- Zhou X, Zhang C, Wu J et al.: Association between *H. pylori* infection and diabetes mellitus: a metaanalysis of observational studies. Diabetes Res. Clin Pract, 99 (2): 200 – 8, 2013.

13- Bytzer P. Talley NJ, Leemon M, et al.: GI Symptoms in diabetes mellitus are associated with both poor glycemic control and diabetic complications. Am J Gastroenterol. 97: 604 – 11, 2002.

14- Talley NJ, Howell S, Jones MP, Horowitz M.: Predictors of turnover of lower gastrointestinal symptoms in diabetes mellitus. Am J Gastroenterol. 97: 3087 – 94, 2002.

15- Abdulbari Bener, Rosetta Micallef, Mustafa Afifi et al.,: Association between

type- 2 diabetes mellitus and *H. pylori* infection: Turk J Gastroenterol. 18 (4): 225 – 229, 2007.

16- Ritzmann S and Daniels: Serum protein abnormalities diagnosis and clinical aspects. Clin. Chem.. Acta. 72: 451 – 461, 1975.

17- Newman AB, Sutton-Tyrrell K, Voget MT, Kullcr LH: Morbidity and mortality in hypertensive adults with a low ankle arm blood pressure index. JAMA, 270: 487 – 489, 1993.

18- Mittelmarke MB, Psaty BM, Fried LP, Borhani No, et al.: Prevalence of cardiovascular disease among older adults: The cardiovascular Health study. Am J Epidemiol, 137: 311 – 317, 1993.

19- O'leary DH, Polak JF, Kronmal RA, Savage PJ et al.,: Thickening of the carotid wall: A marker for atherosclerosis in the elderly. Stroke, 27: 224 – 231, 1996.

20- Vincens Weingart, Holger Russmann, sibylle Koletzko et al.,**:** Sensitivity of a novel stool antigen test for detection of *H. pylori* in adult patient before and after eradication therapy. J Clin Microbiol. 42 (3): 1319 – 1321, 2004.

21- Perez-Perez GI, Rothenbacher D, Brenner H: Epidemiology of *Helicobacter pylori* infection. Helicobacter, 9 (Suppl l): l – 6, 2004.

22- Gentile S, Turco S, Oliviero B, Torella R: The role of autonomic neuropathy as a risk factor of *Helicobacter pylori* infection in dyspeptic patients with type 2 diabetes mellitus. Diabetes Res Clin Pract, 42: 41 – 8, 1998.

23- Xia H-HX, Talley JN, Kam EPY, Young LJ, Hammer J, Horowitz M: *Helicobacter pylori* infection is not associated with diabetes mellitus nor with upper gastrointestinal symptoms in diabetes mellitus. Am J Gastroenterol, 96: 1039 – 1046, 2001.

24- Hamed SA, Amine NF, Galal GM, Helal SR, Tag El-Din LM, Shawky OA, Ahmed EA, Abdel Rahman MS: Vascular risks and complications in diabetes mellitus: the role of *Helicobacter pylori* infection. J Stroke Cerebrovasc Dis. 17 (2): 86 – 94, 2008.

25- Jaber J, Murin J, Kinova S, et al.: The role of infection and inflammation in the pathogenesis of atherosclerosis. Vnitr Lek, 48 (7): 657 – 666, 2002.

26- Gulcelik NE, Kay AE, Demirbas B, et al.: *Helicobacter pylori* prevalence in diabetic patients and its relationship with dyspepsia and autonomic neuropathy. Endocrinol Invest, 28 (3): 214 – 217, 2005.

27- Devrajani BR, Shah SZ, Soomro AA, Devrajani T: Type 2 diabetes mellitus: A risk factor for *Helicobacter pylori* infection: A hospital based case-control study. Int J Diabetes Dev Ctries. 30 (l): 22 – 6, 2010.

28- Ohnishi M, Fukui M, Ishikawa T, Ohnishi N, Ishigami N, Yoshioka K, Hasegawa G, Yoshikawa T, Nakamura N: *Helicobacter pylori* infection and arterial stiffness in patients with type 2 diabetes mellitus. Metabolism. 57 (l2): 1760 – 4, 2008.

29- Fernandini-Paredes GG, Mezones-Holguin E, Vargas-Gonzales R, Pozo-Briceno E, Rodriguez-Morales AJ: In patients with type 2 diabetes mellitus, are glycosylated hemoglobin levels higher for those with *Helicobacter pylori* infection than those without infection? Clin Infect Dis. 47 (l): 144 – 6, 2008.

30- Ming- Chia Hsieh, Sophie S.W. Wang, Yi–Ting Hsieh et al.: *H. pylori* infection associated with high HbAlc and type 2 diabetes. Eur J Clin Invest 43 (9): 949 – 56, 2013.

31- Shin DW, Kwon HT, Kang JM, Park JH, Choi HC, Park MS, Park SM, Son KY, Cho B: Association between metabolic syndrome and *Helicobacter pylori* infection diagnosed by histologic status and serological status. J Clin Gastroenterol. 46 (10): 840 – 5, 2012.

32- Blaser et al., NYU Langon Medical Center: *H. pylori* bacteria linked to blood sugar control in adult type 2DM. Science Daily 2012 March 14. Retrieved sept. 17, 2013.

© 2014 British Journals ISSN 2047-3745

© 2014 British Journals ISSN 2047-3745