Original article:

Dyspepsia among Endoscopy Patients in Two Major Hospitals in Jordan: Correlation with Psychological and Lifestyle Disorders

Sumaia A. N. Shiban¹

Abstract

Background: Dyspepsia is a common complaint, considered as one of the gastrointestinal disorders having a great unfavourable impact on the economic status for countries and individuals, work productivity and quality of life. **Objectives:** The aims of this study are: to estimate the prevalence of dyspepsia among a convenient sample of patients referred for upper endoscopy, to determine the association between dyspepsia and selected different lifestyle and demographic variables, to find out the relationship between dyspepsia and psychological disturbance, and to estimate the prevalence of positive endoscopic findings in comparison to normal (negative) endoscopy. **Materials and Methods:** A cross sectional study included a convenient sample of 460 patients aged 15 or above. Data were analysed and statistical significance determined by Chi- square test at level ($P \leq 0.05$). **Results:** Out of 460 patients, 443 filled the questionnaire completely. The prevalence of dyspepsia among the sample was 59.6%. Among the dyspeptics, endoscopic results showed that functional dyspepsia was more prominent than organic dyspepsia. Variables significantly associated with dyspepsia according to Rome IV criteria were: Age ($P = 0.001$), income ($p = 0.02$), psychological disturbance as stress, anxiety and depression ($p = 0.001$ for each), previous GIT consultation or medication ($p = 0.001$) and H. pylori infection ($p = 0.001$). **Conclusions and Recommendations:** Dyspepsia is associated with a variety of factors. Functional dyspepsia could be prevented by working on lifestyle habits modification and giving more attention towards psychological conditions of patients. Healthcare professionals recommended to identify patient's history more carefully and to proceed with more investigation that is gradual procedures.

Keywords: Dyspepsia, Psychological stress, lifestyle, endoscopic results, Rome IV criteria.

International Journal of Human and Health Sciences Vol. 02 No. 02 April'18 Page : 78-86

Introduction

Gastrointestinal (GI) diseases are responsible for substantial morbidity, mortality and cost. Chronic and recurrent dyspepsia symptoms such as epigastric pain, postprandial fullness, and early satiety are common in the general population. It has a point prevalence of 25–40% even though many sufferers do not seek healthcare¹.

The prevalence in Jordan is 60.1%². In contrast to functional dyspepsia (FD), in which there is no organic cause or lesion found to explain dyspeptic symptoms, organic dyspepsia means that there is a clear pathophysiologic or anatomic reason responsible for dyspeptic complaints³. The exact cause of FD is unknown but it is believed to be related to the noticeable change in lifestyle measures such as more stress, more disturbances

that are psychological, more complicated demographic characters and unhealthy life habits than ever before⁴. Other risk factors include gender, different behavioural characteristics, H. pylori infection, smoking, caffeine intake and ingestion of non-steroidal anti-inflammatory drugs⁴. H. pylori, in particular, is known to be the most common chronic bacterial infection and is more common in developing countries than developed ones. Patients with dyspepsia have a very high prevalence rate of H. pylori infection⁵. Psychological factors are widely believed to have an essential role as a cause of dyspepsia and many other gastrointestinal disorders. Stress, in particular, and history of abuse have been suggested to be important. However, the causative role is yet to be established⁶. Investigations and

Correspondence to: Sumaia A. N. Shiban, MD, Part of Thesis for Master's Science Degree in Public Health- School of Graduate Studies- University of Jordan, Amman-Jordan, Supervised by Professor Dr. Madi Jaghbir E-mail: sumaia_shiban@yahoo.com

treatments for dyspepsia continue to become more sophisticated and expensive. Resources, however; are limited in developing countries and healthcare decision makers are increasingly under pressure to contain costs⁷.

The significance of this study is that no similar studies were conducted in Jordan to highlight the dyspepsia in relation to other factors, even though it is a highly prevalent complaint among the general population locally². Moreover, significant heterogeneity between studies in other countries about dyspepsia and knowledge gap was found regarding the magnitude of risk factors contribution and the pathogenesis.

This study addresses the following objectives: 1) to estimate the prevalence of dyspepsia among a convenient sample of patients referred for upper endoscopy. 2) to determine the association between dyspepsia and selected different life style. 3) To find the association between demographic variables and dyspepsia. 4) to find out the relationship between dyspepsia and psychological disturbance. 5) to estimate the prevalence of positive endoscopic findings in comparison to normal (negative) endoscopy among referred patients.

Materials and Methods

This study is an observational cross section study. A convenient sample of 460 patients referred to the endoscopic departments of two major hospitals in Amman (Islamic Hospital and Jordan University Hospital) were interviewed and asked to fill out a pre-designed self-reported questionnaire. Dyspepsia was assessed objectively through applying ROME IV diagnostic criteria⁸ and psychological disturbances of patients were assessed using depression, anxiety, and stress scale⁹. The endoscopy results were recorded and the findings regarding the presence or absence of any organic pathology were documented.

Inclusion and exclusion criteria:

All patients referred for upper endoscopy were included except the following:

- 1- Patients under the age of 15 years.
- 2- Patients referred from emergency departments for upper endoscopy as emergency cases.
- 3- Inpatient cases already admitted in one of the hospital departments or cases referred to the endoscopy for ERCP (Endoscopic Retrograde Cholangiography) as diagnostic or therapeutic procedure.
- 4- Patients with known psychiatric or medical illnesses or heart attacks.

- 5- Patients known to have either upper GIT tract cancers or cancers anywhere in their body.

Sampling:

The total size of sample was 460 patients. Seventeen of the questionnaires, out of (369) in JUH, were excluded either due to missing data or because patients were found not meeting the study criteria, leaving only 443 for analysis.

Ethical Considerations:

This study had a prior approval from the Faculty of Medicine, Faculty of Graduate Studies Scientific Research Committees. The Ethical approval was gained from the IRB committees of both JUH and Islamic Hospital.

Study instrument and data collection:

The basic information of patients' demographics was recorded and subsequent questions were answered. The prevalence of dyspepsia among involved patients was determined objectively through applying ROME IV diagnostic criteria⁸.

Psychological disturbance of patients was assessed using depression, anxiety, stress scale (DASS21). The endoscopy results of the sample were recorded and the findings regarding presence or absence of any organic pathology were documented. Frequency of depression, anxiety and stress in both groups, i.e. with evidence of abnormal finding at endoscopy and without evidence (normal or normal with gastropathy) was assessed.

Time Frame: The sample collection was carried out from 30/11/2016 and completed on 16/2/2017 in JHH and Islamic hospital, Amman- Jordan.

Study variables:

Endoscopies were performed by gastrologists, and the H. pylori status, if examined, was evaluated using the rapid urease test (RUT). Endoscopic findings, whatever the status of H pylori was, were classified to 3 main categories in which the type of dyspepsia was belonging to:

- 1- Normal Endoscopy: where no abnormal pathological findings were observed.
- 2- Normal endoscopy with associated gastropathy or inflammatory changes: "gastritis" may be accompanied by mucosal injury, while "gastropathy" may show, even if minimal, an inflammatory reaction¹⁰. Practically, the term "gastritis" is often used to describe endoscopic or radiologic characteristics of the gastric mucosa, mostly related to infection, rather than specific histologic findings. Epithelial cell damage and regeneration with minimal or no associated inflammation is properly referred to as "gastropathy"¹¹.

- 3- Abnormal endoscopy: any clear abnormal organic findings. The findings included in this category were: hiatus hernia, peptic ulcers (gastric or duodenal), oesophagitis and GERD, Barrett's oesophagus changes, polyps, masses or swellings, and others such as oesophageal structure, diverticulum or varices.

Data processing and analysis:

Each questionnaire was numbered, data was coded and entered into the computer where it was processed and analysed using Statistical Package for Social Sciences (SPSS, ver.22) software. Variables were analysed using Chi-square test and to find out the significant association between different variables, statistical significance was accepted at level of $p \leq 0.05$.

Results

A total of 443 endoscopy patients aged 15 years or more were included in this study. Table 1 shows the Socio-demographic characteristics of the sample. Mean $\pm$ SD of BMI is 27.7 ± 7.4 and Median (interquartile range) of Income (as Dinar) is 400 (200).

Table 1. Socio-economic characteristics of the patients (n=443)

Variables	n	%
Age (year)		
15 - 40	173	39.1
41 - 65	201	45.4
> 65	69	15.6
Sex		
Male	195	44.0
Female	248	56.0
BMI groups		
Underweight (<18.5)	20	4.5
Normal (18.50 - 24.99)	162	36.6
Overweight (25.00 - 29.99)	137	30.9
Obese class I (30.00 - 34.99)	71	16.0
Obese class II (35.00 - 39.99)	29	6.5
Obese class III (≥ 40)	24	5.4
Marital Status		
Married	304	68.6
Widow	23	5.2
Divorced	7	1.6
Single	109	24.6
Education		
Non-educated	49	11.1
Primary	30	6.8
Secondary or Diploma	229	51.7
University	127	28.7

Variables	n	%
Master	5	1.1
Doctorate	3	0.7
Occupation		
Student	51	11.5
Employed	151	34.1
Unemployed	86	19.4
House wife	86	19.4
Retired	54	12.2
Others	15	3.4
Impression of income status		
Not enough	132	29.8
Accepted	257	58.0
Enough	54	12.2

Regarding lifestyle, the majority of the respondents 336 (75.8%) never smoked cigarettes. Of the patients, Most 340 (76.7%) had never experienced sport exercising and never drank alcohol 438 (98.9%). Meanwhile, 399 (90.1%) of the respondents were coffee and/ or tea drinkers, and 254 (57.3%) used to eating spicy food (Table2). Mean $\pm$ SD of Number of Cigarettes is 21.4 ± 12.2 . Median (interquartile range) of No of pipe/week is 2 (4), median (interquartile range) of exercise/week is 3 (2), median (interquartile range) of coffee/day is 2 (2) and median (interquartile range) of Spicy food/day is 1 (0).

Table 2. Life style of the patients (n=443)

Variable	n	%
Cigarette smoking		
Yes	84	19.0
No	336	75.8
Ex	23	5.2
Pipe smoking		
Yes	38	8.6
No	399	90.1
Ex	6	1.4
Exercise^a		
Yes	103	23.3
No	340	76.7
Alcohol		
Yes	5	1.1
No	438	98.9
Coffee drinking		
Yes	399	90.1

Variable	n	%
No	44	9.9
Spicy food		
Yes	189	42.7
No	254	57.3

(Ex= Previous smoker)

The respondents most frequently had normal stress, anxiety and depression according to DASS scale. In the total study population, mild to extremely severe stress was reported by 52.4%, mild to extremely severe anxiety by 50.8%, and mild to extremely severe depression by 44.0% (Table3).

Table 3. Grades of stress, anxiety and depression according to DASS scale (* n=443)

Grade	Normal		Abnormal							
			Mild		Moderate		Severe		Extremely severe	
	n	%	n	%	n	%	n	%	n	%
Stress*	211	47.6	52	11.7	75	16.9	62	14.0	43	9.7
Anxiety*	218	49.2	32	7.2	73	16.5	38	8.6	82	18.5
Depression*	248	56.0	57	12.9	72	16.3	28	6.3	38	8.6

The endoscopic picture revealed: 49% had normal endoscopy associated with gastropathy or inflammatory changes, 31% revealed abnormal endoscopy, while 20% revealed completely normal endoscopic studies (Figure 1). Biopsies to test for H pylori were taken during endoscopic procedures from nearly 50% of the patients (n = 220).

Sixty percent of the biopsies examined (n = 132) revealed *Helicobacter pylori* positive (Figure 2).

Figure 1. Endoscopic findings among the dyspeptic patients.

Figure 2. H. pylori among the patients (n=220, not done = 223)

Regarding the association between dyspepsia and the other factors, respondent's age and income impression were the only significantly associated socio-demographic characteristics. Some other factors showed association in less degree (Table 4). Respondent's lifestyle habits, like cigarette smoking, alcohol drinking, less exercising, spicy

food and fast food eating (one time/day at least) were more frequent among patients with dyspepsia (more commonly in functional dyspepsia with gastropathy and inflammatory changes) (Table 5). Median income (as Dinar) of each groups are 385 (200), 360 (200), 360 (200) and 400 (200).

Table 4. Association between dyspepsia & demographic characteristics of patients

Variable		No dyspepsia		Dyspepsia with Normal endoscopy		Dyspepsia with normal endoscopy associated with gastropathy or inflammatory changes		Dyspepsia with abnormal endoscopy		<i>P</i>
		n	%	n	%	n	%	n	%	
Age (year)										0.001
	15 – 40	63	36.4	28	16.2	64	37.0	18	10.4	
	41 – 65	85	42.3	38	18.9	46	22.9	32	15.9	
	> 65	31	44.9	7	10.1	12	17.4	19	27.5	
Sex										0.933
	Male	76	39.0	34	17.4	55	28.2	30	15.4	
	Female	103	41.5	39	15.7	67	27.0	39	15.7	
Obesity										0.727
	Yes	54	43.5	17	13.7	33	26.6	20	16.1	
	No	125	39.2	56	17.6	89	27.9	49	15.4	
Marital status										0.625
	Married	122	40.1	46	15.1	86	28.3	50	16.4	
	Not-Married	57	41.0	27	19.4	36	25.9	19	13.7	
		n	%	n	%	n	%	n	%	
Education										0.092
	Primary education or less	31	39.2	20	25.3	16	20.3	12	15.2	
	Secondary education or more	148	40.7	53	14.6	106	29.1	57	15.7	
Occupation										0.198
	Student	22	43.1	11	21.6	10	19.6	8	15.7	
	Employed	62	41.1	28	18.5	46	30.5	15	9.9	
	Unemployed	32	37.2	15	17.4	24	27.9	15	17.4	
	House wife	32	37.2	12	14.0	28	32.6	14	16.3	
	Retired	26	48.1	4	7.4	9	16.7	15	27.8	
	Others	5	33.3	3	20.0	5	33.3	2	13.3	
Impression of income status										0.027
	Not-enough	56	42.4	28	21.2	33	25.0	15	11.4	
	Accepted	108	42.0	31	12.1	76	29.6	42	16.3	
	Enough	15	27.8	14	25.9	13	24.1	12	22.2	

Table 5. Association between dyspepsia and Lifestyle of the patients

Life style		No dyspepsia		Dyspepsia with Normal endoscopy		Dyspepsia with normal endoscopy associated with gastropathy or inflammatory changes		Dyspepsia with abnormal endoscopy		<i>p</i>
		n	%	n	%	n	%	n	%	
Cigarette smoking										0.184
	Yes	24	28.6	14	16.7	30	35.7	16	19.0	
	No	142	42.3	56	16.7	88	26.2	50	14.9	
	Ex	13	56.5	3	13.0	4	17.4	3	13.0	
Pipe smoking										0.460
	Yes	17	44.7	4	10.5	13	34.2	4	10.5	
	No	158	39.6	69	17.3	107	26.8	65	16.3	
	Ex	4	66.7	0	0.0	2	33.3	0	0.0	
Exercise [†]										0.127
	Yes	51	49.5	17	16.5	24	23.3	11	10.7	
	No	128	37.6	56	16.5	98	28.8	58	17.1	
Alcohol										0.421
	Yes	1	20.0	2	40.0	1	20.0	1	20.0	
	No	178	40.6	71	16.2	121	27.6	68	15.5	
Coffee drinking										0.608
	Yes	161	40.4	63	15.8	111	27.8	64	16.0	
	No	18	40.9	10	22.7	11	25.0	5	11.4	
Spicy food										0.638
	Yes	70	37.0	34	18.0	55	29.1	30	15.9	
	No	109	42.9	39	15.4	67	26.4	39	15.4	
Fruit intake										0.431
	<5 times/month	30	38.5	17	21.8	22	28.2	9	11.5	
	2-4 ⁷ week	74	38.7	35	18.3	49	25.7	33	17.3	
	One time at least	75	43.1	21	12.1	51	29.3	27	15.5	
Vegetables intake										0.257
	<5 times/month	26	32.9	13	16.5	28	35.4	12	15.2	
	2-4 ⁷ week	80	42.1	38	20.0	44	23.2	28	14.7	
	One time at least	73	42.0	22	12.6	50	28.7	29	16.7	
Fast food intake										0.507
	<5 times/month	150	42.0	57	16.0	94	26.3	56	15.7	
	2-4 ⁷ week	23	36.5	11	17.5	18	28.6	11	17.5	
	One time at least	6	26.1	5	21.7	10	43.5	2	8.7	

Among 220 patients who were investigated for H pylori, respondents who were H pylori positive were significantly associated with increased risk for development of functional dyspepsia (**Table 6**).

Table 6. Association between dyspepsia and H. pylori (n=220)

Variable	No dyspepsia		Dyspepsia with Normal endoscopy		Dyspepsia with normal endoscopy associated with gastropathy or inflammatory changes		Dyspepsia with abnormal endoscopy		<i>p</i>
	n	%	n	%	n	%	n	%	
H pylori									
Yes	51	38.6	4	3.0	60	45.5	17	12.9	<0.001
No	58	65.9	18	20.5	8	9.1	4	4.5	

Table 7. Association between dyspepsia and psychological disturbance

Variables	No dyspepsia		Dyspepsia with Normal endoscopy		Dyspepsia with normal endoscopy associated with gastropathy or inflammatory changes		Dyspepsia with abnormal endoscopy		<i>p</i>
	n	%	n	%	n	%	n	%	
Stress grade									<0.001
Normal	132	62.6	13	6.2	37	17.5	29	13.7	
Mild	21	40.4	9	17.3	10	19.2	12	23.1	
Moderate	18	24.0	22	29.3	26	34.7	9	12.0	
Severe	7	11.3	16	25.8	29	46.8	10	16.1	
Extremely severe	1	2.3	13	30.2	20	46.5	9	20.9	
Anxiety grade									<0.001
Normal	137	62.8	20	9.2	32	14.7	29	13.3	
Mild	10	31.3	7	21.9	11	34.4	4	12.5	
Moderate	22	30.1	16	21.9	26	35.6	9	12.3	
Severe	5	13.2	6	15.8	16	42.1	11	28.9	
Extremely severe	5	6.1	24	29.3	37	45.1	16	19.5	
Depression grade									<0.001
Normal	147	59.3	20	8.1	47	19.0	34	13.7	
Mild	17	29.8	11	19.3	19	33.3	10	17.5	
Moderate	13	18.1	22	30.6	25	34.7	12	16.7	
Severe	1	3.6	7	25.0	15	53.6	5	17.9	
Extremely severe	1	2.6	13	34.2	16	42.1	8	21.1	

Discussion

The magnitude of dyspepsia as a clinical problem in this study illustrated that more than half of the registered patients for upper endoscopy were complaining from dyspepsia related symptoms with prevalence of 59.6%. Nevertheless, prevalence of dyspepsia in the current study was higher than that of other international studies, which reported a point prevalence ranging from 25% up to 40%. This variation in the findings is most likely depending on the study population, diagnostic criteria, sociocultural issues and symptom definition¹². In addition, the variation in distribution of probable causative factors like that of *H. pylori*, which is highly prevalent in developing countries or psychological variables, might have an effect. However, the prevalence here is nearly the same as that one estimated in a local study conducted in Jordan by Farsakh, et al.² This study results showed that functional dyspepsia accounted for about two-thirds of dyspepsia types. Regarding lifestyle habits and its association with dyspepsia, smoking was insignificantly associated with an increased risk for dyspepsia development. Similarly, smoking had been associated with the development of various gastrointestinal disorders¹³⁻¹⁴. This indicates how much important it is for healthcare workers to emphasize the importance of quitting as an important preventive measure and for salvation of symptoms. In this study, respondents regarding coffee consumption had equal risk for developing dyspepsia. However, coffee may aggravate dyspepsia symptoms in some patients and, if implicated, should be avoided¹⁵. Alcohol intake respondents were insignificantly at high risk for development of dyspepsia. According to Ruigomez, et al.¹³, alcohol has an important role in functional and un-investigated dyspepsia. Regarding *H. pylori*, more than half of the participants who were investigated were found to have *H. pylori* positive results. It is clear that the presence of *H. pylori* significantly increases the probability of getting functional dyspepsia most commonly with gastropathy or inflammatory changes among the respondents. Therefore, *H. pylori* could be tested for early dyspeptic symptoms before the invasive upper GI endoscopy recommendation. Further, this study has shown that the majority of dyspeptic patients were significantly more stressed, anxious or depressed than non-dyspeptic

patients. This study findings suggest that multiple psychiatric disorders in patients with dyspepsia who were referred for upper GI endoscopy are prevalent in our environment as there might be a strong association of psychiatric morbidity with dyspepsia. Nevertheless, these findings suggest that stress was predominantly present in patients with dyspepsia. It is shown that patients with functional dyspepsia (mostly with gastropathy or inflammatory changes) findings on endoscopy have strong significant relation with stress and psychiatric morbidity such as anxiety and depression. These results were concurrent with other studies¹⁶⁻¹⁷.

Conclusions

The estimated degree of relationship between dyspepsia and various risk factors, including psychological disorders and lifestyle disturbances, was in agreement with many published studies from other countries. Most dyspepsia cases have been classified as functional and may need no treatment, except for *H. pylori* infection, which is highly prevalent in this part of the world.

Findings in this, and other similar studies, are good indicators for treating physicians to pursue a conservative approach, with careful history-taking, medical examination and evaluation, rather than referring most patients to undergo endoscopies, unless there are convincing alarm symptoms.

Knowing the prevalence of various types of dyspepsia, and designing appropriate modalities of proper management, is essential to set up priorities, reduce unnecessary diagnostic procedures, minimize pressures on healthcare system and reduce cost.

Patients' counseling towards healthy lifestyles, and proper management of underlying psychological disorders, are instrumental in effective healthcare provision, and avoidance of unnecessary endoscopies.

This study has a number of limitations in view of its observational, cross sectional design, in addition to the observed large variation of definitions and classification of dyspepsia.

Further studies are needed at the wide national level to examine the prevalence and risk factors of dyspepsia in the country, and for the confirmation of these results, it is recommended to examine the validity of Rome IV criteria for diagnosing dyspepsia at clinical settings.

References

1. Benberin V, Bektayeva R, Karabayeva R, Lebedev A, Akemeyeva K, Paloheimo L, Syrjänen K. Prevalence of *H. pylori* infection and atrophic gastritis among symptomatic and dyspeptic adults in Kazakhstan. A hospital based screening study using a panel of serum biomarkers. *Anti Cancer Research*, 2013;33: 4595-4602.
2. Farsakh NA, Saadeh A, Rawshdeh M, Farsakh HA. Dyspepsia in the general population in Jordan. *Indian J Gastroenterol*, 2000;19(2):68-70.
3. Ranjan P. Non-ulcer dyspepsia. *Supplement to Japi*, 2012; 60:13-15.
4. Mahadeva S, Goh KL. Epidemiology of functional dyspepsia: A global perspective. *World J Gastroenterol*. 2006;12(17): 2661–2666.
5. Olokoba AB, Gasha W, Bwala S, Adamu A, Salaw FK. *Helicobacter pylori* infection in Nigerians with dyspepsia. *Ghana Medical Journal*, 2013;47(2):79-81.
6. Tack J, Bisschops R, Sarnelli G. Pathophysiology and treatment of functional dyspepsia. *Gastroenterology*, 2004;127:1239–1255.
7. Moayyedi P, Mason J. Clinical and economic consequences of dyspepsia in the community. *Gut*, 2002; 50:iv10-iv12 doi:10.1136/gut.50.suppl_4.
8. ROMEFoundation(2016),<http://theromefoundation.org/rome-iv/>
9. Lovibond PF, Lovibond SH. Manual for the Depression Anxiety Stress Scales 2nd ed. Sydney, *Psychology Foundation*, 1995a.
10. Kayaçetin S, Güresci S. What is gastritis? What is gastropathy? How is it classified? *Turk J Gastroenterol*, 2014;98:783-788.
11. Feldman M, Jensen PJ. Classification and diagnosis of gastritis and gastropathy. UpToDate 2016.
12. Mahadeva S, Goh KL. Epidemiology of functional dyspepsia: A global perspective. *World J Gastroenterol*, 2006;12(17):2661–2666.
13. Ruigomez A, Garcia Rodriguez LA, Wallander MA, Johansson S, Graffner H, Dent J. Natural history of gastroesophageal reflux disease diagnosed in general practice. *Aliment.Pharmacol.Ther.*, 2004;20:751-760.
14. Aldhous MC, Drummond HE, Anderson N, Baneshi MR, Smith LA, Arnott ID, Satsangi J. Smoking habit and load influence age at diagnosis and disease extent in ulcerative colitis. *Am.J.Gastroenterol*, 2007;102: 589-597.
15. Khademolhosseini F, Mehrabani D, Zare N, Salehi M, Heydari ST, Beheshti M, Saberi-Firoozi M. Prevalence of dyspepsia and its correlation with demographic factors and lifestyle in Shiraz, Southern Iran Middle East. *Journal of Digestive Diseases*, 2010;2 (1):24–30.
16. Xu ZJ, Duan LP, Wang K, Xia ZW, Lin SR. Anxiety and depression related to the symptoms of gastroesophageal reflux disease. *Zhonghuayi Xue Za Zhi*, 2005;30;85(45):3210-3215
17. Aro P, Talley NJ, Ronkainen J, Storskrubb T, Vieth M, Johansson SE, Bolling Sternevald. Anxiety is associated with uninvestigated and functional dyspepsia (Rome III criteria) in a Swedish population-based study. *Gastroenterology*, 2009; 137(1):94-100.