

Prevalence of dyspeptic symptoms and heartburn of adults in Belo Horizonte, Brazil

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ABSTRACT – Background – Medical literature has shown dyspepsia and heartburn-related symptoms occur among 15% to 40% of the population. These symptoms can occur at any age and are more prevalent in women. **Objective** – Investigate the prevalence of dyspeptic symptoms and heartburn among individuals over 18. **Methods** – Individuals over 18 were randomly selected in public venues in Belo Horizonte/MG to participate. A standardized questionnaire that included questions related to social-demographic characteristics, eating habits, digestive symptoms, medical appointments, medications, exams, previous surgeries and comorbidities was applied. A questionnaire about functional dyspepsia diagnosis (Rome III) was also applied. **Results** – A total of 548 individuals were interviewed. Among these, 58.4% were women, 59.3% were white, 55.9% were single and the average age was 36 years. Within this group, 376 individuals (68.6%) declared to have some symptom and/or use medication to relieve dyspepsia symptoms, and for these patients were applied the Rome III questionnaire. Based on the diagnostic criteria for the questionnaire proposed by the Rome III consensus, the symptom of postprandial fullness was reported by 6.7% of the individuals, early satiety (3.5%) and epigastric pain (10.6%). The overlap of these symptoms was very frequent. The prevalence of functional dyspepsia was 10.6% (postprandial discomfort syndrome (8.2%) and epigastric pain syndrome (2.4%). Among all participants, 52.5% reported heartburn, and 11.1% presented this symptom at least once a week. The most used drug was omeprazole. **Conclusion** – The prevalence of dyspeptic symptoms and heartburn among a Brazilian adult urban population is similar to those described in other countries.

HEADINGS – Dyspepsia, diagnosis. Heartburn. Consenso.

INTRODUCTION

The Dyspeptic syndrome is defined by the presence of persistent or recurring pain and/or discomfort, located in the central and upper (epigastrium) abdomen^(1,30,43). These symptoms may result from different diseases such as peptic ulcer, gastric cancer and, most importantly, functional dyspepsia (FD)^(13,17,39,46). These dyspeptic symptoms may also be related to intestinal parasitosis, such as Giardiasis and strongyloidiasis, and in Brazil this may be important for a differential diagnosis⁽³⁴⁾. It affects 25% to 40% of the adults in Western populations (higher prevalence are described in studies that also included heartburn, which is considered a characteristic symptom of the gastroesophageal reflux disease)^(15,18,27). Dyspeptic complaints are responsible for 2% to 5% of outpatient visits in general practitioners, in a primary care center, and 20% to 40% of gastroenterology appointments, and represent a great impact on the quality of life of patients^(1,19,31,46). Dyspepsia is classified as an organic disease (when is secondary to specific lesions, such as esophagitis, peptic ulcer or gastric cancer)⁽²²⁾ or FD (in the absence of structural abnormalities or metabolic and biochemical irregularities that justify the symptoms)⁽¹⁶⁻¹⁸⁾.

An international committee of experts established, in recent years, specific criteria for dyspepsia diagnosis and classification (Rome Criteria), progressing towards the understanding of the syndrome^(12,14,43,44). The Rome consensus suggests the use of specific

questionnaires for FD diagnosis, with a validated version for the local language⁽⁴⁰⁾, which can be used in the diagnostic investigation, by the assistant doctor, or for basic research purposes, but it stresses that physical examination and complementary exams are fundamental to confirm a diagnosis^(16,46).

According to Rome III consensus, the following criteria is required for the diagnosis of FD⁽⁴³⁾: 1) dyspeptic complaints during the last three months and that started at least 6 months before; 2) presence of one or more of the following symptoms: postprandial fullness, early satiety; epigastric pain; epigastric burning; absence of structural lesions in the upper digestive endoscopy.

For better clinical and therapy guidance, patients with FD should be classified, according to their main symptom, in two syndromes⁽⁴³⁾: a) Post-Prandial Distress Syndrome (predominant symptoms are postprandial fullness and/or early satiety, which occurs several times per week in the last 3 months) and/or; b) epigastric pain syndrome (predominant symptoms are epigastric pain or epigastric burning sensation, which is moderate to intense, intermittent, and that occurs at least once a week in the last 3 months).

Population-based studies on this particular topic are rare and, in general, have methodological problems^(24,28) considering the difficulty to exclude structural diseases in a large sample, as required for population studies. Another factor is that the diagnostic criteria for dyspepsia is not standard, although most authors use the criteria suggested by the Rome consensus^(6,29,48).

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A population-based study carried out in southern Brazil⁽⁹⁾ showed a prevalence of 44% of dyspeptic complaints, when using the Rome I criteria⁽¹²⁾ and 19.5% with the Rome II criteria⁽⁴⁵⁾. Dyspeptic symptoms may appear at any age and are more frequent among women, probably due to the fact that the female population seeks medical help quicker^(2,46,49). The intensity of pain and/or discomfort, and anxiety (including the fear of more serious diseases), are the main reasons for seeking a clinical or gastroenterologist opinion.

Heartburn and acid regurgitation symptoms are also common in the Gastroesophageal Reflux Disease (GERD), and are very frequent in daily clinical practice^(4,21,25). The prevalence of GERD is quite variable among the population but is usually high^(5,8,10,25,32).

The objective of this study is to investigate the prevalence of dyspeptic symptoms and heartburn among individuals older than 18 in a Brazilian urban population.

METHODS

Six hundred individuals over 18 were randomly selected in public places within the city of Belo Horizonte/MG, who were invited to participate in the study, and consented their participation according to ethical documentation standards. The individuals answered a questionnaire that included social-demographic characteristics, eating habits, digestive symptoms, medical appointments, medications, exams, previous surgeries and comorbidities. A specific questionnaire for FD diagnosis (Rome III) was applied only among individuals reporting upper digestive tract complaints in the last six months (pain or burning sensation in the chest, pain or burning in the stomach, acid regurgitation, nausea, vomiting, eructation and abdominal fullness) and those who used medication for symptom relief in the last six months.

The Rome III questionnaire is a standardized and trustworthy instrument with a validated version for Brazilian Portuguese⁽⁴⁰⁾.

Eighteen items with ordinal scale responses and individual frequency limits are part of the Rome III questionnaire for dyspepsia. Items 3, 5 and 7 are questions about the frequency of postprandial fullness, early satiety, and epigastric pain or burning sensation symptoms in the last 3 months. Items 4, 6 and 8 shall determine beginning of the symptoms for 6 months or longer with dichotomous responses (yes/no). Items 3 and 5 relate to the diagnosis of postprandial discomfort syndrome (PDS) and items 1, 2, 7, 9, 10 and 12 characterize the epigastric pain syndrome (EPS). Items 11 to 18 show have questions that exclude functional gallbladder and sphincter of Oddi disorder possibilities.

For dyspepsia diagnosis, the proposed scheme drawn up by experts and determined by the consensus⁽⁴³⁾, considering the Rome III questionnaire items⁽⁴⁰⁾, is: I) postprandial fullness: question 3>4, question 4=1; II) early satiety: question 5>4, question 6=1; III) epigastric pain: question 7>3, question 8=1; IV) postprandial discomfort syndrome (PDS): question 3>4, question 4=1, question 5>4, question 6=1. This syndrome includes the symptoms of postprandial fullness and early satiety; V) of epigastric pain syndrome (EPS): question 1<3, question 2<3, question 7>3, question 8=1, question 9>1, question 10>2, question 12=0. This syndrome includes the symptoms of epigastric pain or burning.

The descriptive analysis conducted included distributions of frequencies, central tendency measures and the variability of the characteristics evaluated. The software used for statistical analyses was SPSS® version 19.0. A 5% significance level was considered for all analyses.

The project was approved by the Research Ethics Committee with a presentation ethical assessment certificate (CAAE) number: 04875712.0.0000.5134.

RESULTS

Among 600 participants invited to participate in the study, 548 (91.33%) accepted to participate and 52 (8.66%) were excluded for not agreeing to sign the consent form. Among 548 patients, 320 (58.4%) were women, 325 (59.3%) were white, 307 (56%) were single and 85.6% considered their health condition good/very good. Concerning the educational level of the participants, an average 13.20 years in school (± 3.91) was considered as well as an average age of 36 (± 16.13) years.

Among these, 376 (68.6%) presented some digestive symptom and/or are using medication for symptom relief. Therefore, for these individuals, the Rome III symptom questionnaire was applied. In this group, 232 (61.7%) were women, 226 (60.1%) were white, 213 (56.6%) were single and 83% considered their health condition good/very good. Concerning the educational level of the participants, an average 13.2 years in school (± 3.90) was considered as well as an average age of 35 years (± 15.90) (Table 1).

TABLE 1. Characteristics of 376 individuals interviewed

	n	%	Average (SD)
Gender			
Male	144	38.3	
Female	232	61.7	
Skin color			
Black	27	7.2	
Brown	97	25.8	
White	226	60.1	
Other	26	7.0	
Marital status			
Single	213	56.6	
Married	120	31.9	
Separated	10	2.7	
Divorced	20	5.3	
Widowed	05	1.3	
Other	08	2.1	
Age			35.2 years (± 15.90)
Years of study			13.24 years (± 3.90)
Total	376	100	

SD: standard deviation

The diagnosis criteria in the Rome III questionnaire was used, and the postprandial fullness symptom was reported by 25 individuals (6.7%), early satiety by 13 (3.5%) and epigastric pain by 40 (10.6%). Eight (2.1%) participants reported only postprandial fullness; 24 (6.4%) only complained about epigastric pain and 4 (1.2%) mentioned early satiety. Figure 1 shows the frequent overlap of these symptoms among the symptomatic population.

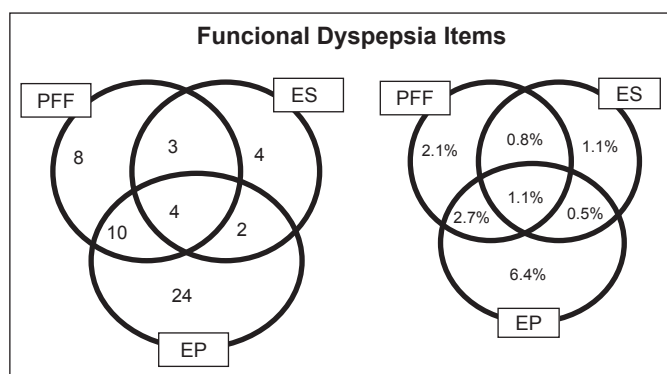


FIGURE 1. Prevalence of postprandial fullness (PPF) symptoms, early satiety (ES) and epigastric pain (EP) with a sample of 376 individuals interviewed in public venues in the city of Belo Horizonte/MG.

By adopting the criteria proposed by the Rome consensus, the prevalence of functional dyspepsia was 10.6%, and 31 (8.2%) participants fulfilled the criteria for the diagnosis of postprandial discomfort syndrome (PDS) (early satiety and/or postprandial fullness) and 9 (2.4%) fulfilled the criteria for epigastric pain syndrome (EPS). There was also a frequent overlap of dyspepsia symptoms observed.

Regarding to the occurrence of heartburn, 40 participants (11.1%) stated that felt it at least once a week, 26 (7.2%) at least twice a week and only two (0.5%) stated that felt discomfort everyday (Table 2).

TABLE 2. Heartburn (discomfort or burning in the chest) occurrence in the last 3 months

Options	N	% Valid	% Cumulative frequency
0 – never	170	47.2	47.2
1 –less than once a month	63	17.5	64.7
2 – once a month	41	11.4	76.1
3 – 2-3 days a month	46	12.8	88.9
4 – once a week	14	3.9	92.8
5 –more than once a week	24	6.7	99.5
6 – everyday	02	0.5	100.0
Total	360	100.0	-

Heartburn or epigastric pain were the most common symptoms, with moderate intensity mostly, that disappeared on the same day and were relieved with medication. Evacuation and changing body positions relieved approximately 50% of individuals. These symptoms were frequently followed by nausea, an uncomfortably “full” feeling after a normal size meal and early satiety.

Life Habits changes (avoid bulky and/or fatty meals, cut off foods containing caffeine or similar, cut down alcohol consumption and the number of cigarettes) in the last 6 months could be observed in both groups, symptomatic and asymptomatic. However, the majority of these changes occurred in the symptomatic group. In this group, 35.4% mentioned they reduced large and/or bulky and/or fatty meals, 23.1% became moderate alcohol consumers and 27.7% reduced their caffeine intake. The majority of patients were non-smokers (76.5%) and among the symptomatic group (64.7%) of the patients who smoke have reported necessity to cut down the number of cigarettes.

The most used medication was omeprazole (39.6%), followed by pantoprazole (9.3%) and antacids (4.8%).

DISCUSSION

In this study, 68.6% of the participants presented symptoms and/or have been using symptom relief medication in the last 6 months. In this group, a higher prevalence of women was observed, which was also described by other studies^(2,28). Higher FD and heartburn prevalence has been observed among women, however, the same finding is not reported for gastroesophageal reflux disease⁽³²⁾.

By adopting the criteria suggested in the Rome III consensus, we observed that the prevalence of FD was 10.6%, and 8.2% met the criteria for the diagnosis of postprandial discomfort syndrome (PDS) (early satiety and/or postprandial fullness) and 2.4% for epigastric pain syndrome (EPS). When evaluating the symptoms independently, postprandial fullness was reported by 6.7%, early satiety by 3.5% and epigastric pain by 10%. A frequent overlap of the dyspeptic symptoms was observed. In this study, 52.8% reported heartburn, and more than 18% have it at least once a week.

According to studies in the United States, Norway, England and other European countries, the prevalence of FD varies between 20% and 40% of the population, with an annual incidence of 1% to 8%^(16,28,29). This variation can be related to geographical differences and the different criteria used to diagnose the disease.

An epidemiological study of adults in Great Britain has demonstrated a 40%⁽³⁵⁾ dyspepsia prevalence. More than half of these individuals were using medication, and 22% of them underwent medical visits in the year prior to the study.

A study conducted in the United States indicated a 31.9%⁽⁴²⁾ dyspepsia prevalence. However, when heartburn cases were excluded (Rome I and II criteria), the prevalence dropped to 15.8%. The most frequent cause of dyspepsia was functional.

In a study carried out in the Czech Republic, 17% prevalence of gastrointestinal symptoms was registered among the general population, and the prevalence of FD was higher among women^(41,47), similar results have been observed in our study.

In Brazil, a study conducted in the southern region, interviewed 3934 individuals, at home, using the Rome II criteria⁽⁹⁾. Frequent dyspepsia was classified as individuals with dyspeptic episodes more than six times per year. The prevalence of dyspepsia was 44.4% and frequent dyspepsia was 27.4%. Among women, dyspepsia was more frequent. When excluding patients with heartburn more than once a week, the prevalence of dyspepsia dropped to 15.9% and frequent dyspepsia to 7.5%⁽⁹⁾.

However, studies performed in the Western world using the Rome III criteria demonstrated that the prevalence of FD lies between 9.8 and 20.2%⁽²⁷⁾, which matches the data obtained in this study.

Another study conducted in northern Sweden indicated a 15.7% prevalence of FD⁽³⁾. The PDS was present in 12.2%, EPS in 5.2% and the overlap of two syndromes was only observed among 1.7% of the population investigated. Finally, a population survey carried out in the region of Minnesota, USA, showed a 15% prevalence of dyspepsia, with 51% of the patients reporting epigastric pain (EPS) and 47% postprandial discomfort (PDS)⁽⁷⁾. Heartburn prevalence was addressed among the symptomatic population and 35.3% had this symptom at least once a month and 11.1% at least once a week⁽⁷⁾.

In Spain, a cross-sectional study identified a 31.6%⁽¹¹⁾ prevalence of GERD. In Belgium, the prevalence observed was 28%⁽²⁶⁾. An Australian study showed that 56% of the individuals reported GERD symptoms at least once in a lifetime, and 37% had these

symptoms at least once every four months⁽⁴⁾. In Denmark, in 1994, the heartburn prevalence was 38% among men and 30% among women⁽²³⁾.

In Southern Brazil, a 48.2%⁽³³⁾ heartburn prevalence was observed, however, among the urban Brazilian population, the prevalence was 11.9%⁽³²⁾. A literature review reported that the variation in the prevalence of these symptoms could range from 10% to 48% (heartburn), 9% to 45% (acid regurgitation) and 21% to 59% for these symptoms combined⁽¹⁹⁾.

A meta-analysis of international studies observed a frequent heartburn prevalence (which occurs at least once per month) between 5% and 20% in the West and up to 5% in East⁽¹⁰⁾, these results are a little lower than those observed in this study.

In a population study carried out in Asia, the authors detected 20.2% of epigastric pain and only 2.1% of heartburn⁽²⁰⁾. The variation observed in different countries can suggest a difference in the gastrointestinal symptom development pattern between the Eastern and Western populations and different diagnosis instruments used.

As the FD and GERD symptoms are often related to the intake of certain foods, this association draws attention. Two studies^(37,38) observed that the ingestion of fatty foods can worsen dyspeptic symptoms, and that postprandial fullness is related to the amount of food ingested and the amount of fat contained in the food. These studies therefore contribute to the findings in this study, since it was observed that 35.4% of the symptomatic patients have reduced bulky and/or greasy meals.

The lifestyle of patients with dyspepsia was evaluated in several studies^(27,28,42), and factors such as smoking and high intakes of caffeine may cause or exacerbate dyspeptic symptoms. This was also observed in this study, since most of the participants who changed their habits regarding caffeine (93.7%) and cigarette (64.7%) consumption belong to the group that presented gastrointestinal symptoms. However, no firm evidence has proven the value of these approaches, and only a minority of patients seem to benefit from these approaches in clinical practice⁽⁶⁾.

Although FD is a very common clinical condition, few prevalence studies were carried out among the general population, especially those adopting the Rome III criteria. As observed in different studies conducted in different countries, a higher prevalence of FD has been observed among women, with a significant variation, and when heartburn symptoms were excluded the prevalence dropped.

The FD prevalence studies present huge variations according to the region, diagnosis criteria and instruments adopted. Generally, the prevalence of FD is lower in the East than the West^(27,28), and greater when the Rome I or II criteria is adopted (especially due to greater symptom periods, which can possibly increase the prevalence)⁽³⁶⁾. Regardless of the data obtained, it is necessary to point out a limitation in these results, that cannot be generalized for the entire population with dyspeptic symptoms and heartburn, because a representative sample has not been used.

CONCLUSION

Dyspeptic symptoms and heartburn are prevalent symptoms in Brazilian adult urban population. The prevalence of FD was in agreement with the latest results from the literature that also used the Rome III criteria. In addition, it has observed that heartburn at least once per month was frequent as observed in other countries. The change of life habits and the use of medication to relieve symptoms were related to the decrease in the symptoms. In general, despite the variation between countries, it was observed that the prevalence of the FD is lower in the East than West greater when adopts Rome I or II criteria, and lower when excluding heartburn.

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Authors' contributions

Almeida AM participated in the study design, data interpretation, manuscript writing, and she revised the final version of the manuscript to be published; Martins LAG participated in the protocol/project development, data collection and manuscript writing/editing; Cunha PLT participated in the protocol/project development, data collection and manuscript writing; Brasil VW participated in the protocol/project development, data collection; Félix LGF participated in the protocol/project development, data collection; Passos MCF participated in the study design, data interpretation, manuscript writing, and she revised the final version of the manuscript to be published. Study supervision: Almeida AM and Passos MCF.

Almeida AM, Martins LAG, Cunha PLT, Brasil VW, Félix LGF, Passos MCF. Prevalência de sintomas dispépticos e de pirose em uma população de adultos em Belo Horizonte, Brasil. *Arq Gastroenterol.* 2017;54(1):46-50.

RESUMO – Contexto – Tem sido relatado que cerca de 15% a 40% da população geral apresenta alguma queixa dispéptica e/ou pirose. Os sintomas dispépticos podem surgir em qualquer idade e são mais prevalentes no sexo feminino. **Objetivo** – Investigar a prevalência de sintomas dispépticos e pirose em indivíduos com idade superior a 18 anos. **Métodos** – Foram selecionados aleatoriamente indivíduos com idade superior a 18 anos, entrevistados em praças públicas de Belo Horizonte/MG, por meio de um questionário que abordou características sócio-demográficas, questões relacionadas aos hábitos alimentares, sintomas digestivos, consultas médicas, medicamentos, exames, antecedentes cirúrgicos, comorbidades e questionário específico para diagnóstico de dispepsia funcional (Roma III). **Resultados** – Foram entrevistados 548 participantes. Destes, 58,4% eram mulheres, 59,3% da raça branca, 56% solteiros e a idade média foi de 36 anos. Neste grupo, 376 indivíduos (68,6%) declararam ter algum sintoma e/ou utilizar algum medicamento para aliviar sintomas dispépticos. Para esses indivíduos, foi utilizado o questionário Roma III para o diagnóstico de dispepsia sendo sintoma de plenitude pós-prandial (6,7%), saciedade precoce (3,5%) e a dor ou queimação no estômago (azia) presente em 10,6%. A sobreposição desses sintomas foi muito frequente. A prevalência de dispepsia funcional foi de 10,6% (síndrome de desconforto pós-prandial (8,2%), síndrome da dor epigástrica (2,4%)). Dentre os participantes, 52,5% relatavam pirose, sendo que desses 11,1% apresentavam este sintoma, no mínimo, uma vez por semana. O medicamento mais utilizado foi o Omeprazol. **Conclusão** – A prevalência dos sintomas dispépticos e pirose na população urbana adulta brasileira é semelhante a descrita em outros países.

DESCRITORES – Dispepsia, diagnóstico. Azia. Consensus.

REFERENCES

1. Agrés L. Natural history of dyspepsia. *Gut*. 2002;50:IV2-9.
2. Ahlawat SK, Cuddihy MT, Locke GR 3rd. Gender-related differences in dyspepsia: a qualitative systematic review. *Gend Med*. 2006;3:31-42.
3. Aro P, Talley NJ, Ronkainen J, Storskrubb T, Vieth M, Johansson SE, et al. Anxiety is associated with uninvestigated and functional dyspepsia (Rome III criteria) in a Swedish population-based study. *Gastroenterology*. 2009;137:94-100.
4. Bolin TD, Korman MG, Hansky J, Stanton R. Heartburn: community perceptions. *J Gastroenterol Hepatol*. 2000;15:35-9.
5. Bretagne JF, Richard-Molard B, Honnorat C, Caekaert A, Barthélemy P. Gastroesophageal reflux in the French general population: national survey of 8000 adults. *Presse Med*. 2006;35:23-31.
6. Camilleri M, Stanghellini V. Current management strategies and emerging treatments for functional dyspepsia. *Nat Rev Gastroenterol Hepatol*. 2013;10:187-94.
7. Choung RS, Locke GR 3rd, Schleck CD, Zinsmeister AR, Talley NJ. Overlap of dyspepsia and gastroesophageal reflux in the general population: one disease or distinct entities? *Neurogastroenterol Motil*. 2012;24:229-34.
8. Cohen H, Tomasso G, Luisa Cafferata M, Zapata C, Sharma P, Armstrong D, et al. Latin american consensus on gastroesophageal reflux disease: an update on therapy. *Gastroenterol Hepatol*. 2010;33:135-47.
9. de Oliveira SS, da Silva dos Santos I, da Silva JF, Machado EC. Prevalence of dyspepsia and associated socio-demographic factors. *Rev Saúde Pública*. 2006;40:420-7.
10. Dent J, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut*. 2005;54:710-7.
11. Diaz-Rubio M, Moreno-Elola-Olaso C, Rey E, Locke GR 3rd, Rodriguez-Artalejo F. Symptoms of gastro-oesophageal reflux: prevalence, severity, duration and associated factors in a Spanish population. *Aliment Pharmacol Ther*. 2004;19:95-105.
12. Drossman DA, Richter JE, Talley NJ, Corazziari E, Thompson WG, Whitehead WE. *Functional gastrointestinal disorders*. Boston, Little Brown 1994.
13. Drossman DA. Functional versus organic: an inappropriate dichotomy for clinical care. *Am J Gastroenterol*. 2006;101:1172-5.
14. Drossman DA. The functional gastrointestinal disorders and the Rome III process. *Gastroenterology*. 2006;130:1377-90.
15. El-Serag HB, Talley NJ. Systemic review: The prevalence and clinical course of functional dyspepsia. *Aliment Pharmacol Ther*. 2004;19:643-54.
16. Ford AC, Moayyedi P. Current guidelines for dyspepsia management. *Dig Dis*. 2008;26:225-30.
17. Ford AC, Moayyedi P. Dyspepsia. *Curr Opin Gastroenterol*. 2013;29:662-8.
18. Hammer J, Talley NJ. Nonulcer dyspepsia. *Curr Opin Gastroenterol*. 2001;17:518-22.
19. Heading RC. Prevalence of upper gastrointestinal symptoms in the general population: a systematic review. *Scand J Gastroenterol Suppl*. 1999;231:3-8.
20. Ho KY, Gwee KA, Khor JL, Selamat DS, Yeoh KG. Validation of a graded response questionnaire for the diagnosis of gastroesophageal reflux disease in an Asian primary care population. *J Clin Gastroenterol*. 2008;42:680-6.
21. Holtmann G. Reflux disease: the disorder of the third millennium. *Eur J Gastroenterol Hepatol*. 2001;13:S5-11.
22. Johnsen R, Bernersen B, Straume B, Førde OH, Bostad L, Burhol PG. Prevalences of endoscopic and histological findings in subjects with and without dyspepsia. *BMJ*. 1991;302:749-52.
23. Kay L, Jørgensen T, Jensen KH. Epidemiology of abdominal symptoms in a random population: prevalence, incidence, and natural history. *Eur J Epidemiol*. 1994;10:559-66.
24. Koloski NA, Talley NJ, Boyce PM. Epidemiology and health care seeking in the functional GI disorders: a population-based study. *Am J Gastroenterol*. 2002;97:2290-9.
25. Kouzu T, Hishikawa E, Watanabe Y, Inoue M, Satou T. Epidemiology of GERD in Japan. *Nihon Rinsho*. 2007;65:791-4.
26. Louis E, DeLooze D, Deprez P, Hiele M, Urbain D, Pelckmans P, et al. Heartburn in Belgium: prevalence, impact on daily life, and utilization of medical resources. *Eur J Gastroenterol Hepatol*. 2002;14:279-84.
27. Mahadeva S, Ford AC. Clinical and epidemiological differences in functional dyspepsia between the East and the West. *Neurogastroenterol Motil*. 2016;28:167-74.
28. Mahadeva S, Goh KL. Epidemiology of functional dyspepsia: a global perspective. *World J Gastroenterol*. 2006;12:2661-6.
29. Mearin F, Calleja JL. Defining functional dyspepsia. *Rev Esp Enferm Dig*. 2011;103:640-7.
30. Moayyedi P. Dyspepsia. *Curr Opin Gastroenterol*. 2012;28:602-7.
31. Monés J, Adan A, Segú JL, López JS, Artés M, Guerrero T. Quality of life in functional dyspepsia. *Dig Dis Sci*. 2002;47:20-6.
32. Moraes-Filho JP, Chinzon D, Eisig JN, Hashimoto CL, Zaterka S. Prevalence of heartburn and gastroesophageal reflux disease in the urban Brazilian population. *Arq Gastroenterol*. 2005;42:122-7.
33. Nader F, da Costa JS, Nader GA, Motta GL. Prevalence of heartburn in Pelotas, RS, Brasil: population-based study. *Arq Gastroenterol*. 2003;40:31-4.
34. Overland MK. Dyspepsia. *Med Clin North Am*. 2014;98:549-64.
35. Penston JG, Pounder RE. A survey of dyspepsia in Great Britain. *Aliment Pharmacol Ther*. 1996;10:83-9.
36. Piessevaux H, De Winter B, Louis E, Muls V, De Looze D, Pelckmans P, et al. Dyspeptic symptoms in the general population: a factor and cluster analysis of symptom groupings. *Neurogastroenterol Motil*. 2009;21:378-88.
37. Pilichiewicz AN, Feltrin KL, Horowitz M, Holtmann G, Wishart JM, Jones KL, et al. Functional dyspepsia is associated with a greater symptomatic response to fat but not carbohydrate, increased fasting and postprandial CCK, and diminished PYY. *Am J Gastroenterol*. 2008;103:2613-23.
38. Pilichiewicz AN, Horowitz M, Holtmann GJ, Talley NJ, Feinle-Bisset C. Relationship between symptoms and dietary patterns in patients with functional dyspepsia. *Clin Gastroenterol Hepatol*. 2009;7:317-22.
39. Quigley EM, Keohane J. Dyspepsia. *Curr Opin Gastroenterol*. 2008;24:692-7.
40. Reisswitz PS, Mazzoleni LE, Sander GB, Francisconi CF. Portuguese validation of the Rome III diagnostic questionnaire for functional dyspepsia. *Arq Gastroenterol*. 2010;47:354-60.
41. Rejchrt S, Koupil I, Kopácová M, Vorisek V, Seifert B, Pozler O, et al. Prevalence and sociodemographic determinants of uninvestigated dyspepsia in the Czech Republic. *Eur J Gastroenterol Hepatol*. 2008;20:898-905.
42. Shaib Y, El-Serag HB. The prevalence and risk factors of functional dyspepsia in a multiethnic population in the United States. *Am J Gastroenterol*. 2004;99:2210-6.
43. Tack J, Talley NJ, Camilleri M, Holtmann G, Hu P, Malagelada JR, et al. Functional Gastrointestinal Disorders. *Gastroenterology*. 2006;130:1466-79.
44. Tack J, Talley NJ. Functional dyspepsia--symptoms, definitions and validity of the Rome III criteria. *Nat Rev Gastroenterol Hepatol*. 2013;10:134-41.
45. Talley NJ, Stanghellini V, Heading RC, Koch KL, Malagelada JR, Tytgat GN. Functional gastrointestinal disorders. *Gut*. 1999;45:II37-42.
46. Talley NJ, Ford AC. Functional Dyspepsia. *N Engl J Med*. 2015;373:1853-63.
47. Vakili N, van Zanten SV, Chang L, Toth G, Sherman J, Fraser M, et al. Comprehension and awareness of symptoms in women with dyspepsia. *Aliment Pharmacol Ther*. 2005;22:1147-55.
48. Van Oudenhove L, Holvoet L, Vandenberghe J, Vos R, Tack J. Do we have an alternative for the Rome III gastroduodenal symptom-based subgroups in functional gastroduodenal disorders? A cluster analysis approach. *Neurogastroenterol Motil*. 2011;23:730-8.
49. Welén K, Faresjö A, Faresjö T. Functional dyspepsia affects women more than men in daily life: a case-control study in primary care. *Gend Med*. 2008;5:62-73.