

What Indigestion Means to the Malays?

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Despite being a large ethnic group within the South-East Asia, there is a paucity of reported literatures on dyspepsia in the Malay population. Recent population-based studies indicate that uninvestigated dyspepsia, based on the Rome II criteria, is reported in 12.8% and 11.6% of Malays in the urban and rural communities respectively. Organic causes of dyspepsia including upper gastrointestinal tract cancers, its precancerous lesions, and erosive diseases are uncommon which is largely due to an exceptionally low prevalence of *Helicobacter pylori* infection in this population. On the other hand, functional dyspepsia and irritable bowel syndrome are relatively common in the Malays than expected. Within a primary care setting, functional dyspepsia, based on the Rome III criteria, is reported in 11.9% of Malays, of which epigastric pain syndrome is found to be more common. Married Malay females are more likely to have functional dyspepsia and psychosocial alarm symptoms. Also based on the Rome III criteria, irritable bowel syndrome, commonly overlapped with functional dyspepsia, is reported in 10.9% of Malays within a community-based setting. Rather than psychosocial symptoms, red flags are most likely to be reported among the Malays with irritable bowel syndrome despite having a low yield for organic diseases. Based upon the above observations, “proton pump inhibitor test” is probably preferable than the “test and treat *H. pylori*” strategy in the initial management of dyspepsia among the Malays.

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Key Words

Dyspepsia; Functional dyspepsia; Irritable bowel syndrome; Malaysia

Introduction

Dyspepsia, a symptom complex centered in the upper abdomen, is a widely known term among clinicians, however, patients often have a variable and inconsistent interpretation of it. Even the commonly used lay term in English, ‘indigestion’ is often vague, encompassing a multitude of poorly defined ills anywhere in the

upper abdomen. Other non-English speaking populations may not have a similar lay term to describe their upper abdominal ills, and this may account for the wide range of prevalence rates reported.¹

South-East Asia is a cultural-diverse region rich with multiple ethnics and indigenous communities. One of the larger ethnic groups is the Malays (*Melayu*) who are a member of the Austronesian family, largely populating the Peninsular Malaysia, Sumatra and Borneo.² The Malay language, has its origin from the an-

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cient Austronesian language, is one of the world most spoken language, being spoken by approximately 180 million people.³

Despite being a large ethnic group within the South-East Asia, there is a paucity of reported literatures on dyspepsia in the Malay population. The current review examined unique characteristics of dyspepsia among the ethnic Malays.

Uninvestigated Dyspepsia

This refers to patients who report dyspeptic symptoms but did not undergo investigations to rule out upper gastrointestinal diseases, including peptic ulcer disease and gastric cancer. Available studies from Asia suggest a frequency of uninvestigated dyspepsia to be between 8-30%, which is clearly variable between different ethnics.⁴ In a cross-sectional survey involving 2,039 multiracial urban population in Malaysia (city of Kuala Lumpur), uninvestigated dyspepsia using the Rome II criteria was reported in 24.3% of adults.⁵ Ethnic Malays comprised 45.3% of the studied urban population and dyspepsia was reported in 12.8%. Among studied risk factors, 56.8% of the Malays had moderate to heavy consumption of chili, 15.7% of the Malays consumed analgesic and only 19.6% had chronic illnesses. A similar cross-sectional survey was performed in 2,000 rural population in Malaysia (Kuala Langat, Selangor), of which uninvestigated dyspepsia using the Rome II criteria was reported in 14.6% of adults.⁶ Ethnic Malays comprise 79% of studied rural population and dyspepsia was reported in 11.6%. There was no significant gender difference (females 15.8% vs. males 12.7%) with or without dyspepsia. Higher levels of education (secondary and tertiary) and non-village type housing were found to be associated with a higher risk for dyspepsia and regular tea drinking appeared to be protective. The rural population frequently reported a lower health-related quality of life but the economic impact of dyspepsia was greater in the urban population.^{6,7} Rural Malays commonly under-report dyspepsia to their doctors and tend to self-medicate.⁸ The level of medical services including endoscopy that is considerably lower in the rural community may be partly responsible for under-reporting.

Organic Causes of Dyspepsia Are Uncommon Among Malays

Helicobacter pylori Infection

Helicobacter pylori infection is responsible for many causes of

organic dyspepsia, in particular peptic ulcer disease and gastric cancer, with important public health consequences. Despite being common among the populations in the Asia Pacific, ethnic Malays are surprisingly spared from this infection. Before the discovery of *H. pylori* in 1982, in the first half of the 20th century, it was already noted that peptic ulcer and gastric cancer were rare in the ethnic Malays but not in the Chinese or Indian populations living in this region.⁹ In a pediatric clinic in Medan, Sumatra, of 874 patients, only 6.5% complained of abdominal pain and 5.5% of abdominal distension.¹⁰ Studies from Singapore also found that the ethnic Malays were under-represented in dyspepsia of any cause in a series of 2,277 patients.¹¹

With the first report of *H. pylori* infection in Malaysia,¹² subsequent studies confirmed that the ethnic Malays have a lower prevalence of *H. pylori* infection compared to the Chinese or the Indian populations (termed the “racial cohort phenomenon”).¹³ The ethnic Malays from the northeastern region of Peninsular Malaysia (state of Kelantan), comprising 90% of its demography, have probably the lowest reported prevalence of *H. pylori* in the world besides the Pemba Island in Zanzibar.¹⁴⁻¹⁷ The *H. pylori* sero-prevalence rate in this region¹⁴ has been reported to be only 4.2% among blood donors and this is in contrast with 11.9% among blood donors in the Klang valley¹³ where the population consists of the Malays of 30% and 15.2% among blood donors in the northwestern region¹⁸ of the Peninsular where the population consists of the Malays of 20%. The above difference in sero-prevalence rates between regions is explained by transmission from *H. pylori*-infected non-Malay immigrants to the non-infected Malays.

The reasons, underlying the low prevalence of *H. pylori* infection among the Malays, remain elusive.¹⁹ One possibility is that local practices or environmental factors may limit transmission or inhibit the infection. In a case-control study involving 161 Malay subjects (79 tested positive for *H. pylori* or “cases” and 82 tested negative for *H. pylori* or ‘controls’) from the state of Kelantan, some dietary factors were found to reduce risk of infection including frequent use of ‘budu,’ ‘pegaga or *Centenella asiatica*’ and tea.²⁰ Unidentified genetic or host factors intrinsic to this population may also result in them being less or have increased susceptibility to *H. pylori* infection or cancer as a whole. In a recent study, protective gene variants were found among ethnic Malays residing in Kelantan including *C7orf10*, *TSTD2*, *SMG7* and *XPA*.²¹ These genes encode enzymes involved in metabolism of compounds which are inhibitory to the survival of *H. pylori* bacterium as well as proteins that allow detection and repair of aberrant genomes. However, polymorphism in the Deleted in

Colorectal Cancer (*DCC*) gene (rs10502974) was associated with increased risk of *H. pylori* infection in the Malays.²²

Upper Gastrointestinal Cancers and Its Precursors

Dyspepsia is one symptom of upper gastrointestinal cancers, often accompanied by alarm features. Due to an exceptionally low prevalence of *H. pylori* among the Malays, gastric cancer and its precancerous lesions are also rare. The incidence of gastric cancer according to the Malaysian National Cancer Registry for the period between 2003-2005 was 2.2/100,000 among the Malays and was lower compared to the Chinese (11.3/100,000) and the Indians (11.9/100,000).²³ In a survey of 234 subjects undergoing upper endoscopy in a tertiary hospital from the state of Kelantan, the overall reported rate of atrophic gastritis was 42.3% (99/234) and that of intestinal metaplasia was 7.7% (14/234).²⁴ Notably intestinal metaplasia was only present in 1.4% (2/146) of Malay subjects. The low rate of atrophic gastritis and intestinal metaplasia in the above study was a result of low *H. pylori* infection in the study population of only 6.8%.²⁴ More recently, certain gene variants are found to be associated with gastric precancerous lesions in this Malay population, and these gene variants, rs9315542 (*UFM1* gene), rs6878265 (*THBS4* gene), rs1042194 (*CYP2C19* gene) and rs10505799 (*MGST1* gene) were associated with atrophic gastritis, complete intestinal metaplasia, incomplete metaplasia with foci of dysplasia and only dysplasia, respectively.²⁵

In contrary to beliefs of some investigator, based on the hypothesis that eradication of *H. pylori* may result in an increase in the incidence of gastroesophageal reflux disease and therefore esophageal cancer, the age-standardized incidence for esophageal cancer among ethnic Malays from Kelantan was only 1.6/100,000 in males and 2.2/100,000 in females.²⁶ Likewise, in a retrospective study involving 1,895 consecutive patients undergoing upper endoscopy between 2005 and 2007 in a tertiary hospital in Kelantan, only 0.8% of patients had Barrett's esophagus.²⁷ The reported rates for Barrett's esophagus are much higher among patients undergoing endoscopy from the northwestern region and the Klang valley of Peninsular Malaysia being 6.2% and 2.0% respectively.²⁷

Gastroduodenal Diseases and Erosive Esophagitis

Early studies from Malaysia indicate that the incidence of peptic ulcers and perforated ulcers were less common among the

Malays, as compared to the Chinese and the Indians.²⁸ Similarly, non-erosive reflux disease and erosive esophagitis remained uncommon in the Malay population, despite a rising trend being observed elsewhere in the region and around the world.^{29,30} In a recent report, clinically significant endoscopic findings, defined as endoscopic pathologies that accounted for symptoms of dyspepsia, were found in 26.4% of Malaysian adults (6.8% in the Malays) with uninvestigated dyspepsia, with risk factors being age \geq 45 years, male gender, *H. pylori* infection and duration of dyspepsia \leq 5 months.³¹ In this study, peptic ulcer disease was found to be more prevalent in the Chinese population and erosive esophagitis in the Indians, but both diseases were not common among the Malays.³¹

Functional Causes of Dyspepsia Are Common in Malays

Rome III Criteria of Dyspepsia

Previously known as non-ulcer dyspepsia, functional dyspepsia (FD), defined by Rome III, is essentially chronic dyspepsia after exclusion of organic diseases.³² In the majority of patients presenting with dyspepsia, often, no underlying organic cause can be identified.⁵ A true prevalence of FD in the general population is however often difficult to determine, but available data from Asia indicate that the prevalence is in the range between 11% and 29%, depending on whether the Rome criteria is used or not.³³ Furthermore, in actual practice, both heartburn and dyspepsia are not easily distinguished from each other, if based on symptoms alone, since overlap frequently exists between the two.³⁴ Likewise, symptoms of irritable bowel syndrome (IBS) frequently coexist with FD, especially in the context of Asia, where patients with IBS tend to report upper abdominal symptoms together.³⁵

There are 4 major symptoms that characterize FD in Rome III, namely, early satiation, postprandial fullness, epigastric pain and epigastric burning, among some of which considerable confusion exists when translated into other languages.³² There have been limited studies on cross-cultural translation of Rome III questionnaires but there are ongoing efforts encouraged by the Rome foundation. Both the Rome III Diagnostic Questionnaires for IBS and FD have been translated into the Malay language, with the IBS module showing reliable psychometric properties during its validation.³⁶ Likewise, the Red Flag and Psychosocial Alarm questionnaires have been translated into the Malay lan-

gauge, although not diagnostic, they are helpful in identifying alarm symptoms, which may alert physicians for further investigations if needed.³⁶ During the translation process, in particular during reconciliation, it is desirable that physicians are involved alongside linguistic experts, and both should be familiar with local nuances. The symptom of fullness and bloating can be particularly challenging during translation with variations regarding especially of its quality, site and severity.

Functional Dyspepsia

The role of *H. pylori* infection in FD has remained unclear.³⁷ Improvement of dyspeptic symptoms has been reported in non-ulcer dyspepsia with eradication of *H. pylori*, especially in the Chinese population but less so in the Western population.³⁸ Part of the problem is that many subjects with non-ulcer dyspepsia might have overlapping *H. pylori*-associated gastritis, which upon eradication leads to some symptom improvement, but true functional symptoms remain. If *H. pylori* infection is contributory to FD, then population with low prevalence of *H. pylori* infection would have reported lesser dyspeptic symptoms, which is apparently not, among the ethnic Malays.

In a cross-sectional survey involving 160 Malay subjects attending primary care clinic in the northeastern region of Peninsular Malaysia, 11.9% fulfilled the Rome III criteria for FD.³⁹ Approximately 2% of subjects were found to have erosive diseases from upper endoscopy but none of the subjects had *H. pylori* infection. This study indicates that FD is more common among the Malays than expected despite the extremely low prevalence of *H. pylori* in this population. A positive married status (odds ratio 8.1) and positive psychosocial alarm symptoms (odds ratio 3.8) were independent risk factors associated with FD. Of those married subjects, females were more likely to have FD and psychosocial symptoms than men. The reasons were likely to be due to a higher divorce rate and the Malay females being the breadwinner rather than men in this region. Of the 2 meal-related syndromes, epigastric pain syndrome (EPS) was found in 68.8% of subjects, especially among married females, and the rest had overlapping postprandial distress syndrome. This was similar to the Muslim population from Pakistan, raising the question, whether if the suppressed role of Muslim females might have played a role.⁴⁰ Furthermore, in the current study, it was found that subjects with FD were more likely obese, which might mean that those with EPS could have gastroesophageal reflux disease. Considering the rather uncommon prevalence of reflux disease in this population, the effect of overlap of gastroesophageal reflux with FD is likely

to be small, but further studies are needed to address this. This study also suggests that *H. pylori* infection is rather a surrogate factor of FD and psychological factors are likely to be more important in its pathogenesis.

Irritable Bowel Syndrome

In a group of 533 (the Malays of 52.2% or 278 subjects) multi-ethnic medical students within the Klang Valley of Peninsular Malaysia, 15.8% of them (the Malays of 15.8% or 44 subjects) were reported to have IBS based upon the Rome I criteria.⁴¹ This urban population from a well-developed economic region was rather young (mean age 22 ± 1.8 years), well-educated and without any chronic illnesses. With such characteristics, it is probably not surprising for this group of population to be prevalent in IBS, similar to previous reports.⁴² In another study involving 949 (the Malays of 33.1% or 314 subjects) multi-ethnic subjects, of mixed urban and rural populations, from the northwestern region of Peninsular Malaysia, based on Rome II criteria, IBS was reported in 15.5% (the Malays of 12.4% or 39 subjects).⁴³ Still part of an economically developed area of the Peninsular, this group of population is relatively older (mean age 33.6 ± 13 years) and contains a mix of rural population. Among 221 ethnic Malays (mean age 37.7 ± 15.7 years), of mixed urban and rural population, from the state of Kelantan, IBS was reported in 10.9% based upon Rome III criteria.⁴⁴ This population was relatively older, had lower socioeconomic power and less educated compared to those Malays in the west coast of the Peninsular. While these studies are community-based rather than population-based, and despite the differences in Rome criteria and socioeconomic status, the prevalence of IBS among the Malays from different regions of the Peninsular is relatively similar, an observation, which is also shared by the population-based data from Singapore.⁴⁵

There was no difference in prevalence of IBS between gender among the Malay population from the state of Kelantan, an observation, likewise being reported from hospital-based studies from India and Sri Lanka.⁴⁶ The reasons for the equivalence in gender prevalence of IBS are unclear and require further studies. Red flags but not psychosocial alarms were commonly reported among subjects with IBS, and it was an independent predictor of IBS after multivariate analysis. Previous reports indicate that red flags have low yield for organic diseases after being investigated,⁴⁷ and this was confirmed in our study subjects with investigated IBS,³⁶ rather its presence was a surrogate for IBS if not diagnostic. However, changing red flags in particular elderly subjects

above 50 years, necessitate further investigations, and this reiterates the importance of follow-up of patients having IBS with red flags.⁴⁸

Conclusion and Relevance to Management

The ethnic Malays, in contrast to the Chinese and Indians, have different characteristics of dyspepsia. Organic causes of dyspepsia, including upper gastrointestinal cancers and erosive diseases, are uncommon among the Malays largely due to a low prevalence of *H. pylori* infection. This epidemiological observation questions the appropriateness of “test and treat *H. pylori*” strategy in this particular population, because it may not be as economical compared to the Chinese or the Indians. However, functional causes of dyspepsia including FD and IBS, are more common than expected in the Malays, and with EPS particularly being common, “empiric therapy with PPI” may be a more appropriate first management strategy rather than the “test and treat *H. pylori*” strategy. Further studies are needed to address this issues. There is equivalence in prevalence between gender, of which reasons are unclear, but males should be given similar attention as females to functional symptoms. Psychosocial alarm symptoms are common among the Malay subjects with FD, particularly among married females, and they should be referred for psychiatric evaluation if deemed necessary. In contrast, red flags are more common among Malay subjects with IBS, and even though they have low yield for organic diseases, nevertheless, they should be followed up regularly and assessed for any changing alarm features, which may necessitate further investigations.

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