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TOPIC HIGHLIGHT

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Epidemiology of functional dyspepsia: A global perspective

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Abstract

Dyspepsia refers to group of upper gastrointestinal symptoms that occur commonly in adults. Dyspepsia is known to result from organic causes, but the majority of patients suffer from non-ulcer or functional dyspepsia. Epidemiological data from population-based studies of various geographical locations have been reviewed, as they provide more realistic information. Population-based studies on true functional dyspepsia (FD) are few, due to the logistic difficulties of excluding structural disease in large numbers of people. Globally, the prevalence of uninvestigated dyspepsia (UD) varies between 7%-45%, depending on definition used and geographical location, whilst the prevalence of FD has been noted to vary between 11%-29.2%. Risk factors for FD have been shown to include females and underlying psychological disturbances, whilst environmental/ lifestyle habits such as poor socio-economic status, smoking, increased caffeine intake and ingestion of non-steroidal anti-inflammatory drugs appear to be more relevant to UD. It is clear that dyspepsia and FD in particular are common conditions globally, affecting most populations, regardless of location.

Key words: Dyspepsia; Uninvestigated dyspepsia; Functional dyspepsia; Prevalence; Epidemiology; Geographical variation

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INTRODUCTION

Dyspepsia refers to a collection of upper gastrointestinal symptoms that is believed to be common world-wide. Despite numerous consensus meetings[1-4], a standardized international definition that is applicable to all populations remains controversial. This is partly due to the overlap with gastro-esophageal reflux disease and the fact that cultural differences remain in reporting of symptoms[5]. The generally accepted definition by most clinicians includes the presence of upper abdominal pain or discomfort with or without other upper gastrointestinal symptoms, such as nausea, belching, vomiting, etc. However, confusion over what patients interpret as abdominal pain versus discomfort continue to "muddy the waters" in this issue[6].

Regardless of its definition, the causes of dyspepsia are known to include peptic ulcer disease, gastro-esophageal reflux, and functional dyspepsia. Functional dyspepsia, otherwise known as non-ulcer dyspepsia, is clearly the commonest cause of dyspeptic symptoms in the West and increasingly in other parts of the world[7]. The latest definition of this includes the presence of "chronic or recurrent pain or discomfort centred in the upper abdomen in the absence of any known structural cause and without any features of irritable bowel syndrome"[4]. The precise pathophysiology of this condition remains unclear, but it is thought to result from a combination of visceral hypersensitivity, gastric motor dysfunction and psychological factors[8].

Functional dyspepsia is not life-threatening and it has not been shown to be associated with any increase in mortality. However, the impact of this condition on patients and health care services has been shown to be considerable. In a recent community survey of several European and North American populations, 20% of people with dyspeptic symptoms had consulted either primary care physicians or hospital specialists, more than 50% of dyspepsia sufferers were on medication most of the time and approximately 30% of dyspeptics reported taking days off work or schooling due to their symptoms[9]. Similar findings have been reported by other leading investigators in this field[10], including the fact that people with functional dyspepsia have a significantly reduced quality of life when compared to the general population[11].

This review aims to describe the epidemiology of func-

tional dyspepsia from a global perspective. Previous reviews on this subject have been based mostly on published reports from Western populations[11,12], mainly as a result of a lack of data from non-Western countries. However, there has been a growth of population-based studies from Asia in the last few years and data from these publications will be emphasised in this review.

POPULATION-BASED STUDIES

In an attempt to demonstrate the variations between populations, we have decided to compare and contrast the prevalence and epidemiology of uninvestigated and functional dyspepsia from various geographical locations. Only studies that have been published in the English medical literature have been selected for this review. Population-based surveys, as opposed to referral-based (for endoscopy) or self-reporting studies, are more representative of the general population as issues such as selection bias (of consulters *vs* non-consulters) are minimized, although not completely excluded. In situations where different population studies from similar or close geographical locations have been presented separately, but have had similar results or conclusions, data from the larger cohort only will be examined in this review.

PREVALENCE OF DYSPEPSIA

The prevalence of dyspepsia varies considerably between different populations (Figure 1). Although these may represent genuine epidemiological differences, it is also apparent that the varying definitions used in different population studies may have contributed to this discrepancy. In studies using "upper abdominal pain" as the definition, the prevalence of uninvestigated dyspepsia (UD) has varied between 7%-34.2%[13,14,22-25,31,32,36]. With this definition, the lowest UD prevalence of 7%-8% is seen in Singapore, South East Asia[31], slightly higher rates are seen amongst the Scandinavians (14.5%[22] and 18.4%)[23,24], prevalence rates of 23-25.8% are seen in the US[13,14] with populations in India (30.4%)[32] and New Zealand (34.2%)[36] having the highest rates.

When a broader definition of "upper gastrointestinal symptoms" is used to define dyspepsia, a 23%-45% prevalence of UD[16-21,26,37] is observed. Using this definition, a lower prevalence is seen in Spain (23.9%)[26], a 32% UD prevalence rate in the US is noted[16], whilst significantly higher rates of 38%-41% are noted in the UK[18-21] and 45% in Nigeria[37].

In population studies that have used the Rome I criteria to define uninvestigated dyspepsia, a prevalence between 18%-38% has been observed[15,29-30,34-35]. The lowest prevalence of 18.4% was recorded in Hong Kong[30], whilst higher rates of 26% and 27.8% were noted in US[15] and Taiwan[29] respectively, and the highest prevalences of up to 38.2% were observed in populations in Australia[34,35].

Finally, with use of the recent Rome II criteria, where symptoms of reflux and IBS are excluded, surveys have reported prevalences around 24%[28,35]. Population studies in Australia and China reported prevalence rates of 24.4%[35] and 23.5%[28] of uninvestigated dyspepsia.

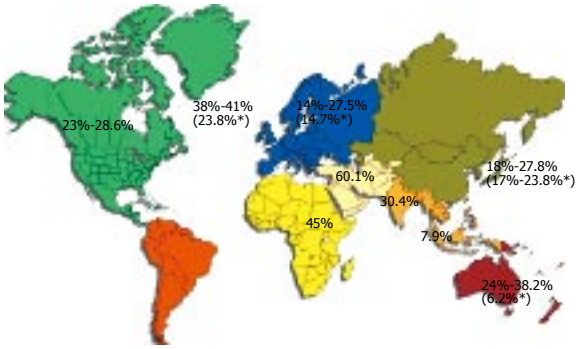

Figure 1 Global prevalence of uninvestigated dyspepsia and functional dyspepsia*.

True functional dyspepsia (FD), where organic disease has been excluded, has been difficult to determine in population studies, for obvious logistical difficulties. Nevertheless, several studies around the globe have actually undertaken this task to provide a reflection of the prevalence of functional or non-ulcer dyspepsia. In a survey of employees within a single institution in the US, Shaib and El-Serag managed to endoscope half of the survey participants and obtained a FD prevalence rate of 29.2% (with reflux symptoms) and 15% (without reflux symptoms)[16]. In the UK, two separate population surveys attempted to estimate the prevalence of FD. One fifth of 9936 subjects surveyed by Jones et al had been investigated with either a Barium meal or endoscopy, and an extrapolated FD prevalence of 23.8% was obtained[18]. Later, in a community survey of 2066 adults, 20% had undergone endoscopy in the study and FD was estimated at 11.5% of this population[19]. A 14.7% of FD was recorded in a Norwegian survey, where the majority of 2027 adults agreed to undergo endoscopy[25]. In Japan, Hirakawa et al were able to document a 17% prevalence of FD in adults undergoing a population gastric cancer screening programme[27]. Finally in Taiwan, the prevalence of FD appeared to vary, depending on criteria used. Of 2018 adults endoscoped, FD was documented at 23.8% with Rome I criteria and confusingly at 11.8% using the Rome II criteria[29].

EPIDEMIOLOGICAL FACTORS

Population-based studies determining the prevalence of dyspepsia have attempted to identify epidemiological risk factors for UD, and when relavant FD as well. Below is a brief summary of various parameters that have been studied in association with the prevalence of dyspepsia.

Age

All surveys that have been conducted have examined adults 18 years or older. While most surveys have shown that dyspepsia does not appear to be related to any particular age group, several studies have noted some trends. Peak prevalences of UD have been noted between the ages 45-54 in a Canadian survey[17], whilst FD appeared to peak in Chinese subjects 41-50 years[28] and in Japanese adults 50-59 years[27]. In the latter study, dyspepsia sub-types appeared to be associated with different age groups: reflux-like more common in middle-aged adults, dysmotility-like more

frequent in those < 59 years and ulcer-like predominant symptoms more frequently in adults < 39 years. In other populations, the prevalence of UD appeared to decrease with increasing age in British[18], Taiwanese[29] and Danish[23] surveys. In the latter survey, there was a significantly lower prevalence of UD in adults > 70 years (10%) compared to those < 60 years (18.4%)[23]. In contrast, a survey in urban Mumbai, India found that UD was more prevalent in adults > 40 years[32]. Despite these trends, age extremities has not been identified as a predictor of dyspepsia (UD or FD).

Gender

Most population studies have been able to obtain relatively equal ratios of male: female ratios and the majority of them have shown no differences in dyspepsia prevalence between genders, mostly where UD is concerned. Several studies, in different populations, however, have noted a consistent female preponderance with dyspepsia[16, 23, 26, 29,34]. Female gender was found to be the only independent risk factor for FD amongst 2018 Taiwanese health check attendees[29]. In a population-based study in Australia, female adults significantly outnumbered males in most functional GI disorders, including FD[34]. As only a few population studies have examined true FD prevalence, it is likely that the gender effect in surveys of UD have been masked due to the combination of adults with FD and organic dyspepsia.

Ethnicity

The role of ethnicity in dyspepsia has not been examined by most population studies. Most surveys have been done on populations of single/similar ethnic groups, mostly of Caucasian or Oriental background (Table 1). However, in one of the few studies involving subjects of several ethnic backgrounds from a single institution in the US, African-American race was found to be one of several epidemiological risk factors for UD[16]. In a survey of a multi-racial population in Singapore, South East Asia, the ethnic-adjusted prevalence of UD was demonstrated as follows: Chinese 8.1%, Malays 7.3% and Indians 7.5%[31]. Although the majority ethnic group in Singapore is Chinese, the authors were able to obtain prevalence based on equal representations of the three different ethnic groups. At present, little can be concluded regarding the role of ethnicity and it is clear that more data is required from future studies.

Smoking

Although a common practice world-wide, regular smoking as a risk factor has not been consistent in its association with dyspepsia. In the few population-based studies that have examined FD, smoking has not been shown to be a risk factor[25,28,29,34]. In surveys of patients with UD however, regular smoking has been identified as a risk factor in populations in US[16], Canada[17], UK[21] and India[32]. This observation may be explained by the proportion of organic disease amongst subjects with UD, as smoking has been identified as clear risk factors for diseases like peptic ulcer disease[38].

Alcohol

Regular alcohol intake, as a risk factor, has been studied and it has not been shown to be associated with dyspepsia in the vast majority of surveys. However, in the Asia-Pacific region, only population studies in India[32] and New Zealand[36] have showed definite associations between alcohol and UD.

Non-steroidal anti-inflammatory drugs

The effect of non-steroidal anti-inflammatory drugs (NSAIDs) on dyspeptic symptoms have been examined specifically in only two population-based studies. In a survey of American adults from a single institution, regular usage of NSAIDs and Aspirin, bought over the counter, were strongly associated with UD than in controls without dyspepsia[16]. In a British study of 4982 adults, NSAID usage was identified as an independent risk factor for UD and thought to be responsible solely for 4% of dyspepsia in the community[21]. Interestingly, data from the African sub-continent may correlate this fact in a study of Nigerian highlanders. "Indulgence in self-medication" amongst the subjects surveyed was found to be a significant risk factor for UD[37]. Although this was not described clearly, and probably included various types of traditional medication, it is probable that analgesics containing NSAIDs may account for a sizeable amount of this "self-medication".

Helicobacter pylori infection

To date, only one population-based study in the UK has investigated the association of *H pylori* infection with UD. Among 8047 subjects who were tested for *H pylori,* those who were infected had more dyspeptic symptoms (44%) than those who were *H pylori* negative (36%)[21]. Subsequent analysis revealed *H pylori* status to be predictive of UD and the authors concluded that *H pylori* infection had a 5% population attributable risk for dyspepsia assuming a causal association. The association of *H pylori* and FD is less clear, but this has only been examined in some detail in non-population-based studies[39].

Dietary factors

The role of diet in dyspepsia has not been studied by many, probably due to the diversity of dietary habits within individual populations. In the few studies that have attempted to examine dietary factors and their association with dyspepsia, the definitions of food types and categories do not appear to be clear. In the Chinese study examining the prevalence of FD[28], "bad dietary habits" was shown to be a significant risk factor. However, the authors fail to clarify their definition of this term. In an urban survey in India, Shah et al managed to demonstrate that no differences in dyspeptic symptoms occurred between vegetarians (29.1%) and meat-eaters (31.2%), whilst spicy, fried or food prepared outside the home contributed insignificantly to worsening of symptoms[32]. In Nigerian adults living in the highlands, the type of staple food consumed was strongly associated with UD, but no specific definitions of food types are given[37]. The effect of caffeine intake has also been examined in some population studies,

Table 1 Epidemiology of uninvestigated dyspepsia (UD) and functional dyspepsia (FD)

Location	*n*	Population	Ethnicity	Age (yr)	Definit on of dyspepsia	Prevalence UD	Prevalence FD	Gender difference	Risk factors
N. America									
US [13]	1021	One county	Caucasian	30-64	Upper abdominal pain	25.8%	NA	None	NA
US[14]	919	One county	Caucasian	30-49	Upper abdominal pain	23%	NA	None	Sexual abuse Physical abuse
US[15]	8250	National	Caucasian	49.1 (mean)	Rome I	26%	2.7%	None	< 45 yr age Lower income Being employed
US[16]	465	One institution	Black 46% Caucasian 36%	44.6 (mean)	Upper GI symptoms	31.9%	29.2%	Yes (F > M)	Black ethnicity NSAIDs Smoking
Canada[17]	1036	12 Cities	Not stated	18-80	Upper GI symptoms	28.6%	NA	None	Low socio-economic status Life events Smoking Cola
Europe									
UK[18]	9936	National	Caucasian	20-69	Upper GI symptoms	41%	23.8% (estimate)	None	NA
UK[19]	2066	2 Communities	Caucasian	20-80	Upper GI symptoms	38%	11.5%	None	NA
UK[21]	9262	2 counties	Not stated	40-49	Epigastric pain ± upper GI symptoms	38%	NA	None	Low socio-economic status *H pylori* infection Smoking
Europe									
Sweden[22]	1422	One municipality	Caucasian	20-87	Upper abdominal pain	14.5%	NA	None	NA
Denmark[23,24]	4581	One county	Caucasian	30-60	Epigastric pain	16.2% (M) 20.8% (F)	NA	Yes (F > M)	Psychological disorder Social problems
Norway[25]	2027	One municipality	Caucasian	20-69	Upper abdominal pain	27.5%	14.7%	None	Family history Tranquiliser usage
Spain[26]	284	One city	Not stated	18-80	Upper GI symptoms	23.9%	NA	Yes (F > M)	None
Asia									
Japan[27]	911	1 city	Japanese	18-70	Upper GI symptoms	NA	17%	None	NA
China[28]	1016	Health check attendees	Chinese	15-75	Rome II	NA	23.5%	None	Poor diet Low socio-economic status Societal pressure Past abuse Anxiety/depression
Taiwan[29]	2018	Health check attendees	Chinese	18-80	Rome I Rome II	27.8%	23.8% 11.8%	Yes	Female gender
Hong Kong[30]	1649	National	Chinese	37.9 (mean)	Rome I	18.4%	NA	None	Anxiety/depression
Singapore[31]	706	1 Community	Chinese 8.1% Malays 7.3% Indians 7.5%	21-95	Upper abdominal pain ± upper GI symptoms	7.9%	NA	None	NA
India[32]	2549	One city	Indian	18-80	Upper abdominal pain	30.4%	NA	None	Alcohol Smoking
Jordan[33]	2254	One county	Arabic	> 16 yr	Not stated	60.1%	NA	None	NA
Australasia									
Australia[34]	2910	One city	Not stated	43.8 (mean)	Rome I	38.2%	6.2%	None	Female gender Anxiety/ depression
Australia[35]	2300	One city	Not stated	> 18	Rome I Rome II	32.5% 24.4%	NA	None	NA
New Zealand[36]	952	community	Not stated	> 18	Recurrent upper abdominal pain	34.2%	NA	None	Alcohol Aspirin use
Africa									
Nigeria[37]	1151	community	African		Upper GI symptoms	45%	NA	None	Family size Occupational scatter Type of food Melaena Self medication

particularly from Western studies. Surveys in the US and Europe have reported that excessive coffee or tea intake has not been shown to be related to the presence of dyspepsia/UD[16,17,21,23,25]. However, in one of the few studies to examine its' role, a Canadian survey showed that heavy intake of cola was associated with markedly increased prevalence of dyspepsia[17]. An explanation for this observation may be due to the fact that greater quantities of caffeine in cola can be consumed more readily, or it may be a non-caffeine related compound which is responsible for dyspeptic symptoms. Clearly, more studies on the role of diet in dyspepsia are needed, but standardization in dietary terminology and habits are required before meaningful conclusions can be elicited from such data.

Socio-economic associations

Most population-based studies have examined basic socio-demographic associations in dyspepsia and the majority have not revealed any significant findings, eg between social classes and prevalence of dyspepsia. However studies examining details of socio-economic status were able to elicit associations with dyspepsia. Drossman in the US noted a strong relationship between lower household income and larger household membership with increased functional GI diseases, including FD[15]. Similarly, a Canadian survey revealed that chronic GI symptoms (UD) were more prevalent in adults with lower household income, those who were unemployed and with lower educational levels[17]. In a British survey, factors including rented accommodation, no central heating, low educational level and sharing a bed with siblings (surrogate for crowded household) were found to be predictive of UD in adults[21]. Amongst an urban population of dyspeptics in China, "dissatisfaction with financial income" was associated with FD, but this was not as significant as other psychological factors (see below)[28]. Finally, in the Nigerian study, a larger sized family together with occupational scatter was strongly associated with UD[37].

Psychological associations

In most population surveys that have studied psychological disturbances as a risk factor, definite risk associations, particularly for FD, have been elicited. Talley *et al* had previously reported in an American adult population that sexual, emotional and verbal abuse either in childhood or adulthood were significantly associated with dyspepsia[14]. This, in turn resulted in more health-care seeking behaviour amongst this group of adults. In a Danish survey, Kay and Jorgensen noted that UD was strongly associated with adults who had "experience of problems" and "psychological vulnerability"[23]. In one of the few population-based studies that managed to examine FD in some detail (by excluding structural abnormalities in most of the adults), the authors found that FD patients, as opposed to those with UD alone had a significant association with tranquiliser usage[25], probably a surrogate marker for anxiety or a neurotic behaviour. This observation is similarly observed in an Australian survey where adults with FD scored highly on anxiety and depression scales[34], and in a Chinese study which revealed "pressure from society" and "destructive living habit" as risk factors for FD[28]. Yet another survey in Hong Kong also revealed that subjects with UD had more anxiety, compared to adults with IBS, which appeared to influence health-care seeking habits[30].

Summary

Table 1 summarises the features of the epidemiology of dyspepsia from a geographical perspective. The published data to date supports the notion that dyspepsia is common in most populations of this world. The varying prevalence of UD in different populations, some even in similar geographical locations, appear to be related to the different definitions of dyspepsia used by investigators of individual surveys. The true prevalence and epidemiology of FD amongst the general population has not been evaluated as much, due to the difficulties in excluding organic disease in large numbers of people. Nevertheless, several studies[16,25,27,29] have been able to examine this in some detail. With the data that is available, the true prevalence of FD globally is estimated between 11.5%-29.2% (including symptoms of reflux) (Figure 1). Epidemiologically, it appears that risk factors for FD are different to that of organic dyspepsia and even general UD. Where this has been studied in some detail, female gender and underlying psychological disturbances have been shown to be important factors in FD[16,25,28,29,34]. In contrast, environmental/lifestyle habits such as poor socio-economic status, smoking, increased caffeine intake and NSAID ingestion appear to be more relevant to UD[17,21,28,32] . We believe this is a result of the presence of organic disease in these populations. Although a peak preponderance of dyspepsia around the middle ages (40-50 years) have been reported in some surveys[26,27], the extremities of age do not appear to be predictive of dyspepsia generally. Apart from one study from the US[16], the role of ethnicity has not been shown to be relevant. However, most of the published surveys have usually been on single/majority ethnic populations and hence this factor has yet to be refuted for certain.

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