Frequency of Painful Physical Symptoms With Major Depressive Disorder in Asia: Relationship With Disease Severity and Quality of Life

Phil Lee, M.D.; Mingyuan Zhang, M.D.; Jin Pyo Hong, M.D.; Hong-Choon Chua, M.B.B.S., M.Med. (Psychiatry); Kuang-Peng Chen, M.D.; Siu Wa Tang, M.B.B.S., Ph.D.; Benjamin T. M. Chan, M.D.; Min Soo Lee, M.D.; Bobbie Lee, M.Sc.; Gabrielle L. Gallagher, Ph.D.; and Martin Dossenbach, M.D.

Objective: Patients with major depressive disorder (MDD) frequently report concomitant painful physical symptoms, which may negatively impact diagnosis and treatment. The purpose of this study was to estimate the frequency of painful physical symptoms in Asian patients treated for an acute episode of MDD and to describe the associated demographics, clinical status, treatment patterns, and socioeconomic burden.

Method: This multicountry, observational study enrolled 909 patients with MDD (DSM-IV-TR or ICD-10 criteria) in the psychiatric care setting from June 14, 2006, to February 15, 2007. Patients were classified as positive for painful physical symptoms (PPS+) if they achieved a mean score ≥ 2 on the modified Somatic Symptom Inventory. The Clinical Global Impressions-Severity of Illness scale (CGI-S) and 17-item Hamilton Rating Scale for Depression ($HAM\text{-}D_{17}$) determined depression severity, and the EuroQoL Questionnaire-5 dimensions (EQ-5D) assessed subjective well-being.

Results: Overall, 51.8% of patients were classified as PPS+. PPS+ patients were more likely to be female (72.2% vs. 65.1%, p = .022), had relatively more medical comorbidity (29.7% vs. 21.0% with ≥ 1 comorbidity, p = .003), were more significantly depressed (CGI-S mean [SE] score = 4.84 [0.03] vs. 4.63 [0.04], p < .001; $HAM\text{-}D_{17}$ mean [SE] score = 24.80 [0.26] vs. 22.39 [0.27], p < .001), and reported a lower quality of life (EQ-5D health state mean [SE] score = 42.96 [0.92] vs. 52.92 [0.95], p < .001) than PPS– patients. PPS+ and PPS– patients did not differ markedly, however, in terms of MDD medications prescribed or MDD-related disability at work.

Conclusion: Painful physical symptoms are experienced by approximately half of patients with MDD in Asia and are associated with poor clinical status and perceived quality of life.

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Corresponding author and reprints: Gabrielle L. Gallagher, Ph.D., Intercontinental Information Sciences, Eli Lilly Australia Pty Ltd, Level 1, 16 Giffnock Ave., Macquarie Park NSW 2113, Australia (e-mail: gallagherga@lilly.com).

Major depressive disorder (MDD) is a psychiatric illness that encompasses both emotional and physical symptoms. The condition affects an estimated 340 million people worldwide,[1] yet despite its high prevalence, MDD is speculated to be underdiagnosed. Recognition of MDD may be compromised due to the high incidence of concomitant painful physical symptoms, which can mask underlying emotional symptoms.[2,3] In fact, up to half of all patients seeking help for active depression may go undiagnosed because they present with somatic or physical symptoms rather than the classic emotional symptoms of depression.[4]

Prevalence of physical pain in depressed persons ranges from 15% to 100% (mean = 65%),[5] varying widely based on the definition of pain condition. Within MDD

populations, sociodemographic characteristics such as age, female gender, and lower level of education have been found to predict comorbid pain.[6,7] Ethnicity, too, may influence the somatic presentation of depression,[7–9] with some studies suggesting that patients in non-Western or developing countries report physical symptoms and deny emotional symptoms more frequently than patients in Western and developed countries. In Asia, the frequency of painful physical symptoms in patients with MDD is currently unknown; however, "somatization" of depression may account, at least in part, for the consistently lower MDD prevalence reported in Asian countries.[10–13]

The quantification of painful symptoms in patients with MDD is relevant to both patient diagnosis and treatment. Comorbid pain is associated with poor depression outcomes, including more severe depression, worse self-rated quality of life, worse productivity, prolongation of help-seeking, and increased health care utilization.[6,14–16] More importantly, treatment of physical symptoms and improvement in pain outcomes are associated with higher probability of remission.[17]

The purpose of this study was to estimate the frequency of painful physical symptoms in Asian patients who are treated for an acute MDD episode by a psychiatrist in a naturalistic, clinical practice setting. Additional objectives included description of the associated demographics and comparison of baseline clinical status, antidepressant prescription patterns, and work-related disability associated with MDD, within the full cohort and between participants with and without painful physical symptoms.

METHOD

Study Population

Inpatients and outpatients at least 18 years of age who presented with a new or first episode of MDD, as defined by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR),[18] or the *International Classification of Diseases and Related Health Problems, 10th Revision* (ICD-10),[19] and were prepared to take antidepressant medication, were considered eligible for study entry. Additional inclusion criteria were as follows: Clinical Global Impressions-Severity of Illness scale (CGI-S)[20] score ≥ 4 (moderately ill) at study entry; at least 2 months free of depressive symptoms prior to the onset of the current episode; and consent to release of data.

Patients were excluded if their current episode of depression had been persistent for more than 6 continuous months; if they had a previous or current diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, bipolar disorder, or dementia; if they were experiencing chronic, treatment-resistant pain or a painful condition of inflammatory origin related to an identifiable medical condition; or if they were simultaneously participating in another study that included treatment intervention or investigational drug.

Study Design

This prospective, non-interventional, epidemiologic study was designed to assess the frequency of painful physical symptoms in Asian patients treated for an acute episode of MDD in naturalistic, clinical practice settings. The study enrolled 909 patients from 40 study sites across 6 Asian countries and regions: China, Hong Kong, Korea, Malaysia, Singapore, and Taiwan. Patients were recruited from June 14, 2006, to February 15, 2007, and individual patients were followed for a period of 3 months. All patients who satisfied the entry criteria and agreed to participate in the study were enrolled up to the sample size allocated. No further selection or stratification was involved.

This article presents baseline data of all enrolled patients. Assessment and treatment decisions were based solely on the health care provider's routine or usual practice in the provision of care to patients with MDD.

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices. The institutional or ethical review board of at least 1 site in each participating country approved the study, and consent to release information was received from each patient or from the patient's legal representative prior to enrollment.

Measures

Demographic and clinical data, including prior course of MDD, antidepressant and other MDD medication prescribed, concomitant pain medication prescribed, and current medical conditions (comorbidities), were collected at the baseline visit. Comorbidity information was collected for 10 predefined conditions considered of particular interest: alcohol abuse, alcohol dependence, cardiovascular disease, cervical/lumbar disease, chronic movement disabilities, diabetes mellitus, gastrointestinal disorder, renal disease, substance abuse, and substance dependence. For patients who were employed within the 3 months prior to study entry, the impact of their depression-related illness on work productivity (for example, hours worked and days absent from work) was evaluated through a questionnaire.

Patients were assessed at study entry for the presence or absence of painful physical symptoms (PPS+ and PPS–, respectively), defined by a mean score ≥ 2 on the pain-related items of the modified Somatic Symptom Inventory.[21] The Somatic Symptom Inventory evaluated how much the patient had been "bothered" from "not at all" (1 point) to "a great deal" (5 points) over the previous week. Patients with and without painful physical symptoms were compared in subsequent analyses.

Table 1. Demographic Characteristics and Disease History for the Total Study Population and the Painful Physical Symptom Positive (PPS+) and Painful Physical Symptom Negative (PPS–) Subgroups

Characteristic	PPS+ (N = 471)	PPS– (N = 438)	Total (N = 909)	p Value
Age, mean (SD), y	45.2 (14.1)	45.1 (14.2)	45.1 (14.1)	.887[a]
Gender, female, N (%)	340 (72.2)	285 (65.1)	625 (68.8)	.022[b]
Ethnic origin, N (%)				.806[c]
East Asian	469 (99.6)	435 (99.3)	904 (99.5)	
West Asian	2 (0.4)	2 (0.5)	4 (0.4)	
White	0 (0.0)	1 (0.2)	1 (0.1)	
Country, N (%)				NA
China	105 (22.3)	194 (44.3)	299 (32.9)	
Hong Kong	66 (14.0)	24 (5.5)	90 (9.9)	
Korea	91 (19.3)	107 (24.4)	198 (21.8)	
Malaysia	63 (13.4)	35 (8.0)	98 (10.8)	
Singapore	12 (2.6)	18 (4.1)	30 (3.3)	
Taiwan	134 (28.5)	60 (13.7)	194 (21.3)	
BMI, mean (SD), kg/m^2	23.11 (4.2)	22.72 (3.6)	22.92 (3.9)	.147[a]
Duration of current depressive episode, median (range), wk[d]	8 (1–53)	8 (1–52)	8 (1–53)	.148[e]
1 or more previous episodes, N (%)[f]	205 (45.0)	194 (44.6)	399 (44.8)	.946[b]
No. of previous episodes, median (range)	1 (1–18)	2 (1–11)	2 (1–18)	.277[e]
Time between remission of last and start of current episode, median (range), wk[d]	40 (2–832)	48 (4–676)	43 (2–832)	.526[e]
Seasonal pattern to episodes, N (%)[f,g]	9 (15.8)	8 (13.3)	17 (14.5)	.796[b]

[a]p Value using t test for comparisons of means.
[b]p Value using Fisher exact test.
[c]p Value using extension of Fisher exact test.
[d]Patients with MDD episode duration less than 2 weeks or greater than 6 months or with remission duration less than 2 months were identified during data analyses; however, the small number of patients did not impact the overall study results.
[e]p Value using nonparametric Wilcoxon rank sum test.
[f]Percentages based on the 891 (of 909) patients reporting this variable.
[g]Only measured in patients with 3 or more previous episodes.
Abbreviations: BMI = body mass index, MDD = major depressive disorder.

The severities of overall pain, headache, back pain, shoulder pain, interference of pain with daily activities, and time awake in pain were quantified by means of 100-mm visual analog scales (VAS). The pain severity VAS was anchored by "no pain" to "as severe as I can imagine"; the interference VAS was anchored by "none" to "complete"; and the time in pain VAS was anchored by "none" to "all the time."

Severity of depression was determined using the CGI-S and the 17-item Hamilton Rating Scale for Depression ($HAM\text{-}D_{17}$).[22] The anxiety/somatization subscale (sum of items: anxiety [psychic], anxiety [somatic], somatic symptoms/gastrointestinal, somatic symptoms/general, hypochondriasis, and insight) and core mood subscale (sum of items: depressed mood, feelings of guilt, suicide, work and activities, and retardation) of the $HAM\text{-}D_{17}$ were also assessed. Patient perception of quality of life and health status was assessed using the EuroQoL Questionnaire-5 Dimensions (EQ-5D)[23] scale, which included statements related to mobility, self-care, usual activities, pain/discomfort, and anxiety/depression ("Utility" score) and a visual analog scale ("Health State" score).

Training and assessment (rating of a videotaped patient interview) were performed to ensure consistency between investigators with respect to rating of the $HAM\text{-}D_{17}$. A maximum variation of +3 or –3 from the prespecified $HAM\text{-}D_{17}$ total score was considered acceptable, and, in addition, 60% agreement with the 17 individual items was required. Investigators with scores outside the acceptable range were retrained until an adequate level of consistency with other raters was achieved.

Statistical Analysis

Descriptive statistics were used to characterize patients at study entry. Baseline characteristics were compared across painful physical symptom groups using 2-sample t test or nonparametric Wilcoxon rank sum test for continuous variables and Fisher exact test for categorical variables. Continuous clinical outcome variables (VAS, CGI-S, $HAM\text{-}D_{17}$, and EQ-5D) were compared across painful physical symptom groups using 1-way analysis of variance. All statistical analyses were performed using SAS Version 8.2 for Windows (SAS Institute, Inc., Cary, N.C.). No adjustment for multiple comparisons was performed since secondary analyses were considered supportive. The level of statistical significance was defined a priori as 2-sided p value of .05.

RESULTS

Patient Demographics, Disease History, and Comorbidities

A total of 909 patients with MDD were enrolled across 6 Asian countries/regions, and almost all patients (99.5%,

Table 2. Comorbidities of the Total Study Population and the Painful Physical Symptom Positive (PPS+) and Painful Physical Symptom Negative (PPS–) Subgroups

Variable	PPS+ (N = 471)	PPS– (N = 438)	Total (N = 909)	p Value[a]
No. of listed comorbidities, N (%)				
0	331 (70.3)	346 (79.0)	677 (74.5)	.003[b]
1+	140 (29.7)	92 (21.0)	232 (25.5)	
Comorbidity, N (%)				
Cardiovascular disease	59 (12.5)	45 (10.3)	104 (11.4)	.299
Gastrointestinal disorder	51 (10.8)	22 (5.0)	73 (8.0)	.001
Diabetes mellitus	25 (5.3)	20 (4.6)	45 (5.0)	.648
Cervical/lumbar disease	25 (5.3)	5 (1.1)	30 (3.3)	< .001
Alcohol abuse	11 (2.3)	8 (1.8)	19 (2.1)	.648
Renal disease	13 (2.8)	2 (0.5)	15 (1.7)	.007
Chronic movement disabilities	7 (1.5)	5 (1.1)	12 (1.3)	.775
Alcohol dependence	3 (0.6)	4 (0.9)	7 (0.8)	.717
Substance abuse	1 (0.2)	1 (0.2)	2 (0.2)	> .99
Substance dependence	2 (0.4)	0 (0.0)	2 (0.2)	.500

[a]p Value using Fisher exact test.
[b]p Value using Fisher exact test to compare distribution of 0 versus 1+ comorbidities.

N = 904) were of East Asian origin (Table 1). Mean (SD) age of patients was 45 (14) years, and 68.8% were female. Almost half of the patients enrolled (44.8%) had experienced 1 or more previous MDD episodes, and median duration of the current episode was 8 weeks. The median time interval between remission of the last episode and onset of the current episode was 43 weeks, and of the patients with 3 or more previous episodes, 14.5% reported a seasonal pattern to their episodes. Approximately three quarters of patients (74.5%) did not currently have any of the comorbidities of interest (Table 2), the most common of which were cardiovascular disease (11.4%, N = 104), gastrointestinal disorder (8.0%, N = 73), and diabetes mellitus (5.0%, N = 45).

Frequency of Painful Physical Symptoms

The presence of painful physical symptoms was determined by a mean score ≥ 2 on the pain-related items of the Somatic Symptom Inventory (Table 3). At baseline, 471 patients (51.8%) were classified as PPS+. The proportion of female patients was higher in the PPS+ group compared with the PPS– group (72.2% vs. 65.1%, respectively, p = .022); however, no differences were observed in terms of MDD disease history. A relatively higher number of PPS+ patients reported at least one comorbidity (29.7% vs. 21.0%), and the specific conditions reported more frequently by PPS+ patients were gastrointestinal disorder (10.8%, N = 51 vs. 5.0%, N = 22), cervical/lumbar disease (5.3%, N = 25 vs. 1.1%, N = 5), and renal disease (2.8%, N = 13 vs. 0.5%, N = 2). Few patients reported alcohol and substance dependence or abuse, and no difference was observed between PPS+ and PPS– groups for these conditions.

Table 3. Frequency of Painful Physical Symptoms for the Positive (PPS+) and Negative (PPS–) Subgroups for the Overall Study Population and by Individual Country/Region

Category	PPS+, N	PPS–, N	Total, N	PPS+ Frequency, % (95% CI[a])
Overall	471	438	909	51.8 (48.5 to 55.1)
China	105	194	299	35.1 (29.7 to 40.8)
Hong Kong	66	24	90	73.3 (63.0 to 82.1)
Korea	91	107	198	46.0 (38.9 to 53.2)
Malaysia	63	35	98	64.3 (54.0 to 73.7)
Singapore	12	18	30	40.0 (22.7 to 59.4)
Taiwan	134	60	194	69.1 (62.1 to 75.5)

[a]Binomial exact CI.

While the overall frequency of painful physical symptoms in this Asian sample was 51.8% (95% CI = 48.5% to 55.1%), individual country frequency varied (Table 3). Mainland China reported the lowest PPS+ frequency (35.1%) in this study, approximately half that reported by Hong Kong (73.3%) and Taiwan (69.1%). In addition, PPS+ frequency in Singapore (40.0%) was lower than in neighboring Malaysia (64.3%), although the sample population in Singapore was small (30 patients total), and the confidence intervals wide (95% CI = 22.7% to 59.4%).

The distribution of pain severity for pain-related items of the Somatic Symptom Inventory is displayed in Figure 1. Muscle soreness and headaches were the most common pains experienced by both PPS+ and PPS– patients, and these were also the most severe, with over 20% of the total patient population indicating they had been bothered "a great deal" or "quite a bit" during the previous week. Patient-rated pain severity across the various VAS domains also demonstrated a similar pattern for PPS+ and PPS– groups (Figure 2). Notably, PPS+ patients reported spending over 55% of their time awake in pain, and this pain interfered considerably with daily activities.

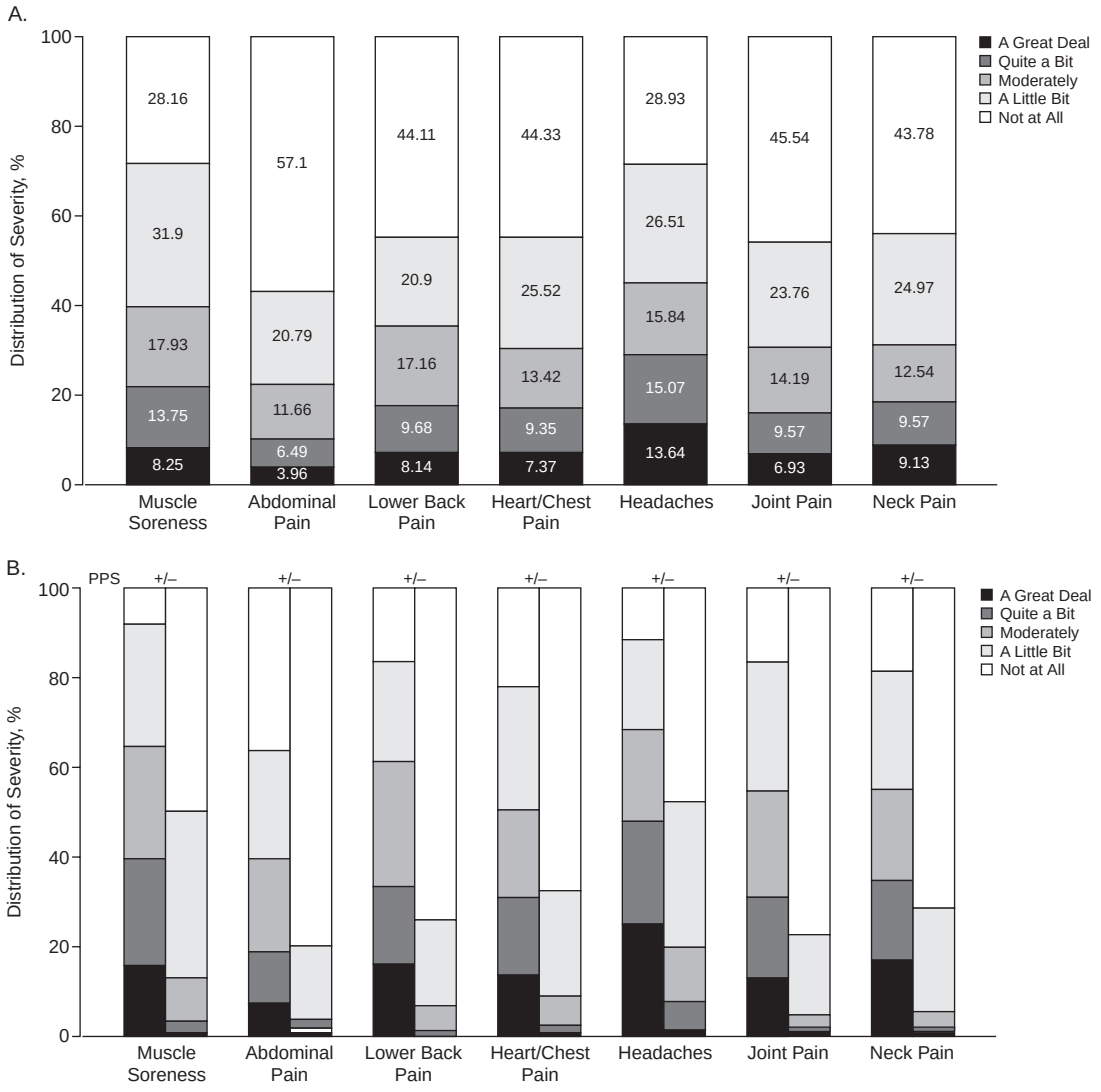
Clinical Status

The clinical status of patients at baseline is summarized in Table 4. The presence of painful symptoms was associated with greater depression severity: CGI-S mean difference 0.21 (95% CI = 0.11 to 0.30, p < .001) and HAM-D_{17} mean difference 2.41 (95% CI = 1.68 to 3.15, p < .001). In addition, patients with painful symptoms rated their quality of life significantly lower than patients without (mean difference = –9.95, 95% CI = –12.55 to –7.36, p < .001), as measured by the EQ-5D health state score.

Treatment Patterns

Of the 909 patients included in this study, 816 (89.8%) were prescribed antidepressant medication at study entry

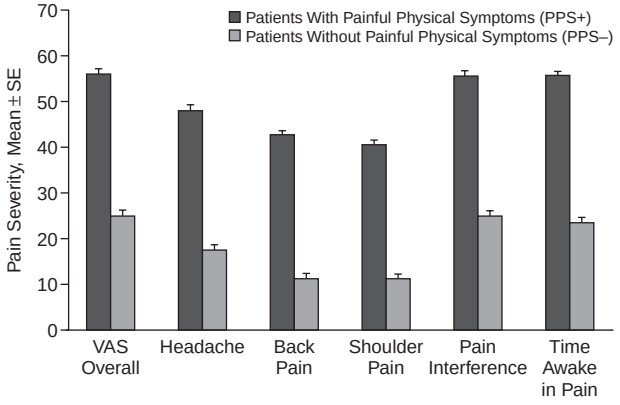
Figure 1. Patient Response to the Pain-Related Items on the Somatic Symptom Inventory for the Total Population (A) and the Painful Physical Symptom Positive (PPS+) and Painful Physical Symptom Negative (PPS–) Subgroups (B)



(Table 5). The majority of patients (81.2%) were prescribed monotherapy, and the most commonly prescribed classes of antidepressant were selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and noradrenergic and specific serotonergic antidepressants (NaSSAs; mirtazapine was the sole antidepressant of this class). No statistically significant differences were observed in the proportion of PPS+ versus PPS– patients prescribed SSRIs or SNRIs; however, a greater proportion of PPS+ patients were prescribed NaSSAs (mirtazapine; 13.4% [N = 63] vs. 8.2% [N = 36], p = .014).

The 10 most commonly prescribed antidepressants were (in order of frequency) fluoxetine, paroxetine, venlafaxine, escitalopram, mirtazapine, sertraline, trazodone, citalopram, bupropion, and duloxetine. Fewer PPS+ than PPS– patients were prescribed paroxetine (11.0% [N = 52] vs. 20.1% [N = 88], p < .001), while more PPS+ than PPS– patients were prescribed duloxetine (4.3% [N = 20] vs. 1.6% [N = 7], p = .019) and mirtazapine (as described above). No differences between PPS+ and PPS– patients were observed in terms of concomitant medication prescribed for MDD; however, as expected, more PPS+ than PPS– patients used concomitant pharmacotherapy for pain (11.2% [N = 52] vs. 4.2% [N = 18], p < .001). Massage was the most frequently used nondrug therapy for pain, and although patient numbers were small (1.9% [N = 17]), there was a statistically significant difference between PPS+ and PPS– groups (2.8% [N = 13] vs. 0.9% [N = 4], p = .049).

Figure 2. Mean Pain Severity as Measured by Visual Analogue Scale (VAS) for Painful Physical Symptom Positive (PPS+) and Painful Physical Symptom Negative (PPS–) Subgroups[a]



[a]p < .001 between subgroups for all domains; p value using type III sums of squares from 1-way analysis of variance. Significant differences were expected because the 2 groups were classified on the basis of painful physical symptoms.

Impact of Depression-Related Illness on Work

In total, 528 (58.2%) patients reported they had not worked in the 3 months prior to study entry (Table 6). Of the patients who had worked, only 11.4% (N = 43) reported that they were unhindered by health problems related to MDD. Patients worked, on average, approximately 40 hours per week over the prior 3 months, but were absent from work due to MDD-related illness a median of 4 days (range, 0–90 days). The extent of disability to work was not statistically significantly different for PPS+ and PPS– patients.

DISCUSSION

This study reports, for the first time, that the frequency of painful physical symptoms in patients with an acute episode of MDD in Asia is 51.8%. This result lies within the range reported for North America (69%),[14] Europe (43%),[24] and Latin America (73%)[25] and provides further evidence that painful, physical manifestations of depression are globally widespread.

Previous speculation that non-Western cultures are more likely to somatize depression is not supported by this study. It should be noted, however, that frequency of painful physical symptoms reached as high as 73.3% in Hong Kong, but the relatively low frequency of 35.1% reported in China, the country with the largest sample population, substantially affected the overall result. Previous literature suggests Chinese patients are among the most likely to identify physical symptoms of depression, rather than emotional, as their primary complaint.[9,26] This may result, however, in many patients with MDD and comorbid painful symptoms seeking consultation from another medical specialist, such as a neurologist (rather than a psychiatrist), or simply remaining undiagnosed. Variance between individual countries may also arise due to different recruitment practices; while all eligible patients were invited to participate in the study (that is, consent to the release of information), certain centers may have more "aggressively" recruited patients in physical distress.

The higher proportion of women reporting painful physical symptoms in this Asian MDD population is consistent with other ethnicities.[6,25] An association between age and the presence of painful physical symptoms has also been reported previously[6,7]; however, no such relationship was observed in the present study. This concurs with findings that age and prevalence of MDD (with or without comorbid pain) are not proven to be related in Asian countries,[12,13] in contrast to North America and Europe.[27,28]

Patients with painful physical symptoms in this study were more likely to report a current comorbidity; however, more than 70% of patients with painful symptoms could not attribute their pain to any of the conditions listed. Demyttenaere and coworkers[6] reported that, for the general population, the presence of major depression results in a 2-fold increase in painful physical symptom prevalence for those both with and without a comorbid somatic disorder. Depression may therefore amplify both medically explained and unexplained painful symptoms, and the presence of pain in patients with somatic disorders may not necessarily be attributable to that condition.

The presence of painful physical symptoms in this population was associated with more severe depression, as measured by CGI-S and HAM-D_{17}. This relationship has been consistently reported across ethnicities,[6,7,25] and several possible explanations exist. The coexistence of physical discomfort may lead to increased psychological distress; that is, patients are more severely depressed because they experience pain. However, it is also possible that severe depression may lower the threshold at which patients become aware of pain ("somatosensory amplification")[29]; that is, patients experience pain because their depression is more severe. Indeed, the 2 conditions may be physiologically linked through their shared neurobiology (such as serotonin and norepinephrine neurotransmission), and are in fact 2 sides of the same coin.[30]

Despite the difference in depression severity between PPS+ and PPS– patients, no significant difference was observed in the number of antidepressants prescribed at baseline. This most likely reflects the acute nature of MDD onset in this study; approximately half of the patients presented with their first episode and were therefore likely to be treated conservatively upon diagnosis. There were some minor differences in the type of antidepressant prescribed, including the more frequent prescription of mirtazapine and duloxetine to PPS+ patients.

Table 4. Clinical Status (CGI-S, HAM-D_{17}) and Quality of Life (EQ-5D) for Painful Physical Symptom Positive (PPS+) and Painful Physical Symptom Negative (PPS–) Subgroups

Measure	PPS+ (N = 471), Mean (SE)	PPS– (N = 438), Mean (SE)	Difference, Mean (95% CI)	p Value[a]
CGI-S	4.84 (0.03)	4.63 (0.04)	0.21 (0.11 to 0.30)	< .001
HAM-D_{17} total	24.80 (0.26)	22.39 (0.27)	2.41 (1.68 to 3.15)	< .001
HAM-D_{17} anxiety/somatization	8.60 (0.12)	7.31 (0.13)	1.29 (0.95 to 1.63)	< .001
HAM-D_{17} core mood	9.58 (0.12)	8.76 (0.13)	0.82 (0.47 to 1.17)	< .001
EQ-5D health state	42.96 (0.92)	52.92 (0.95)	–9.95 (–12.55 to –7.36)	< .001
EQ-5D utility[b]	0.37 (0.01)	0.61 (0.02)	–0.24 (–0.28 to –0.20)	< .001

[a]p Value using type III sums of squares from 1-way analysis of variance.
[b]An Asian norm for the EQ-5D utility score is not available, thus the results can only be used in relative terms.
Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, EQ-5D = EuroQol Questionnaire-5 Dimensions, HAM-D_{17} = 17-item Hamilton Rating Scale for Depression.

Table 5. Antidepressant and Pain Medication Treatment Patterns for the Total Study Population and the Painful Physical Symptom Positive (PPS+) and Painful Physical Symptom Negative (PPS–) Subgroups

Variable	PPS+ (N = 471)	PPS– (N = 438)	Total (N = 909)	p Value[a]
No. of antidepressant medications used, N (%)				
0	36 (7.6)	57 (13.0)	93 (10.2)	.457[b]
1	396 (84.1)	342 (78.1)	738 (81.2)	
2+	39 (8.3)	39 (8.9)	78 (8.6)	
Antidepressant medication class, N (%)[c]				
SSRI	260 (55.2)	264 (60.3)	524 (57.7)	.123
SNRI	86 (18.3)	65 (14.8)	151 (16.6)	.181
NaSSA	63 (13.4)	36 (8.2)	99 (10.9)	.014
Concomitant treatment for MDD, N (%)[d]				
No treatment	144 (30.7)	127 (29.1)	271 (29.9)	.612
Pharmacotherapy	315 (67.2)	296 (67.7)	611 (67.4)	.887
Antipsychotics	55 (11.7)	54 (12.4)	109 (12.0)	.838
Benzodiazepines	308 (65.7)	279 (63.8)	587 (64.8)	.578
Mood stabilizers	14 (3.0)	10 (2.3)	24 (2.7)	.542
Nondrug therapies[e]	61 (13.0)	66 (15.1)	127 (14.0)	.389
Concomitant treatment for pain, N (%)[f]				
No treatment	393 (84.9)	403 (93.7)	796 (89.1)	< .001
Pharmacotherapy	52 (11.2)	18 (4.2)	70 (7.8)	< .001
Combination[g]	5 (1.08)	0 (0.00)	5 (0.56)	.063
Herbal medicines	9 (1.94)	3 (0.70)	12 (1.34)	.147
NSAIDs	39 (8.42)	15 (3.49)	54 (6.05)	.002
Opioids	1 (0.22)	0 (0.00)	1 (0.11)	> .99
Nondrug therapies[h]	20 (4.3)	9 (2.1)	29 (3.3)	.087

[a]p Value using Fisher exact test.
[b]p Value using Fisher exact test to compare distribution of 0 versus 1+ antidepressant medications.
[c]Other classes of antidepressant medication prescribed (but not shown) include tricyclic (4.6%), tetracyclic (4.2%), dopamine reuptake inhibitor (3.3%), and monoamine oxidase inhibitor (0.3%).
[d]Percentages based on the 906 (of 909) patients reporting this variable.
[e]Nondrug therapies for MDD included psychosocial therapy (11.8%), electroconvulsive therapy (2.4%), light therapy (0.2%), and sleep deprivation therapy (0.1%).
[f]Percentages based on the 893 (of 909) patients reporting this variable.
[g]Combination products, for example acetaminophen with opioid.
[h]Nondrug therapies for pain included massage (1.9%), relaxation techniques (1.2%), acupuncture (0.3%), and acupressure (0.2%).
Abbreviations: MDD = major depressive disorder, NaSSA = noradrenergic and specific serotonergic antidepressant, NSAIDs = nonsteroidal anti-inflammatory drugs, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

Table 6. Impact of Depression-Related Illness on Work for the Total Study Population and the Painful Physical Symptom Positive (PPS+) and Painful Physical Symptom Negative (PPS–) Subgroups

Variable	PPS+ (N = 471)	PPS– (N = 438)	Total (N = 909)	p Value
Patient did not work, N (%)[a]	278 (59.1)	250 (57.2)	528 (58.2)	
Average hours worked per week (per patient)				
Number reporting	190	183	373	
Mean (SD)	40.3 (17.6)	39.4 (14.8)	39.9 (16.3)	.592[b]
Problems related to MDD at work				
Number reporting	192	187	379	
No, not at all, N (%)	18 (9.4)	25 (13.4)	43 (11.4)	
Yes, to a degree, N (%)	109 (56.8)	110 (58.8)	219 (57.8)	
Yes, very much, N (%)	65 (33.9)	52 (27.8)	117 (30.9)	.222[c]
Days absent from work due to MDD				
Number reporting	191	185	376	
Median (range)	3 (0–90)	4 (0–60)	4 (0–90)	.887[d]

[a]Percentages based on the 907 (of 909) patients reporting this variable.
[b]p Value using t test for comparisons of means (patients who were employed only).
[c]p Value using Fisher exact test to compare distribution of "yes, very much" versus others combined (patients who were employed only).
[d]p Value using nonparametric Wilcoxon rank sum test.
Abbreviation: MDD = major depressive disorder.

While presentation of painful symptoms will not be the only factor influencing prescription patterns (for example, availability of specific agents in each country may vary), this prescribing practice may be a reflection of recent evidence that antidepressants targeting both serotonin and norepinephrine are more effective in alleviating physical pain associated with depression, and with achieving remission in such patients.[17] In spite of this awareness, however, over 80% of patients reporting painful symptoms were not prescribed concomitant medication for pain, suggesting management of somatic complaints by Asian psychiatrists remains relatively unaggressive.

As may be expected, patients with painful physical symptoms rated their quality of life to be poorer than those without painful physical symptoms. No significant difference, however, was observed between the groups in terms of work-related disability. This is in contrast to

Demyttenaere and coworkers,[6] who demonstrated an additive effect of depression and painful symptoms on "Work Loss Days" score in European MDD patients. Similarly, the National Health Interview Survey of Disability (North America) found the proportion of respondents unable to work with a mental condition only, a general medical condition only, or with both were 25.8%, 34.8% and 61.1%, respectively.[31] It is possible that differing results reflect cultural attitudes to work; Asian patients with MDD may be reluctant to admit any negative impact on productivity given the high regard for work ethic in their culture.[32]

There are a number of limitations that need to be considered when interpreting these data. While the present study quantified the frequency of painful physical symptoms in Asian patients with MDD, it did not ascertain how likely patients are to volunteer this information of their own accord, that is, without a questionnaire such as the Somatic Symptom Inventory. Asian patients may not experience more painful symptoms of depression than other ethnicities; however, it remains unknown if they are more likely to identify pain as their primary complaint and deemphasize emotional symptoms. Parker and coworkers[9] found that while depressed Chinese Malaysian patients were more likely than Caucasian Australian patients to present volunteering somatic symptoms, when provided with a symptom inventory made up of somatic and cognitive items, little differentiation in affirming somatic items was evident. Sample differences emerged, in fact, less from differences on the somatic factor and more from differences on the cognitive factor.

Supplemental value may have been added to this study had information regarding comorbid anxiety disorders been collected. There is increasing evidence that painful symptoms are not specific to depression, but are also increased with anxiety. A recently published population-based study from Europe found approximately 45% of persons with anxiety disorder also reported the presence of painful physical symptoms.[33] It would be of interest, as a future investigation, to assess the frequency of painful physical symptoms in patients with MDD and anxiety disorder in this Asian population.

An additional limitation of the present study is that painful physical symptom frequency is restricted to the (inpatient and outpatient) psychiatric care setting only. Literature suggests that for Western cultures, painful symptoms are equally as common, or slightly less so, in the primary care setting.[5,6] However, as speculated in this report, the primary care setting may not be the only void for Asian countries (such as China) if patients seek consultation directly from neurologists, or are directed to neurologists from general practitioners. Future epidemiologic studies representing (1) all medical care settings and (2) the general population (community) may be of value, particularly in Asia.

CONCLUSION

The results of this study demonstrate that painful physical symptoms are experienced by approximately half of patients treated for an acute episode of MDD in the psychiatric care setting in Asia. Painful symptoms are associated with worse clinical status and perceived quality of life, suggesting management of physical manifestations, in addition to emotional, may lead to improved treatment success.

Drug names: bupropion (Aplenzin, Wellbutrin, and others), citalopram (Celexa and others), duloxetine (Cymbalta), escitalopram (Lexapro and others), fluoxetine (Prozac and others), mirtazapine (Remeron and others), norepinephrine (Levophed and others), paroxetine (Paxil, Pexeva, and others), sertraline (Zoloft and others), venlafaxine (Effexor and others).

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