

ORIGINAL ARTICLE

Physical comorbidities in older adults receiving antidepressants in Asia

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Abstract

Background: The present study explored the patterns of physical comorbidities and their associated demographic and clinical factors in older psychiatric patients prescribed with antidepressants in Asia.

Methods: Demographic and clinical information of 955 older adults were extracted from the database of the Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) project. Standardized data collection procedure was used to record demographic and clinical data.

Results: Proportion of physical comorbidities in this cohort was 44%. Multiple logistic regression analyses showed that older age (OR = 1.7, $P < 0.001$), higher number of depressive symptoms (OR = 1.09, $P = 0.016$), being treated in psychiatric hospital (OR = 0.5, $P = 0.002$), living in high income countries/territories (OR = 2.4, $P = 0.002$), use of benzodiazepines (OR = 1.4, $P = 0.013$) and diagnosis of ‘other psychiatric disorders’ (except mood, anxiety disorders and schizophrenia) (OR = 2.7, $P < 0.001$) were significantly associated with physical comorbidities.

Conclusions: Physical comorbidities in older patients prescribed with antidepressants were common in Asia. Integrating physical care into the treatment of older psychiatric patients should be urgently considered.

Key words: antidepressant, Asia, older adults, physical comorbidity.

INTRODUCTION

With decreasing birth rates and increasing life expectancy, the proportion of older adults has been growing globally. For example, the percentage of older adults in Europe is expected to rise to 44% by 2025.¹ Psychiatric disorders are very common in the older adult population. In Europe, 47% of older adults experienced at least one psychiatric disorder in their lifetime, and nearly one-fourth had a current psychiatric disorder.² Lifetime prevalence of any type of psychiatric disorder was 23% in older African Americans.³

Use of antidepressants is becoming more prevalent in older adults in recent years,⁴ particularly in developing countries.⁵ This could be partly because of the increased identification of depressive symptoms, treatment initiation and maintenance treatment in depressed patients.⁶ Another reason could be the increased off-label use of antidepressants for other conditions, such as chronic physical illness, mild cognitive impairment or functional limitation.⁷

Aging is associated with increased risk of both chronic physical diseases and psychiatric disorders. Older adults with major psychiatric disorders including depression, schizophrenia and bipolar disorder have a particularly high risk of physical comorbidities, such as hypertension (83.1%), diabetes mellitus (43.1%), congestive heart failure (29.0%) and chronic obstructive pulmonary disease (27.5%).⁸ Physical comorbidities with psychiatric disorders could result in poor quality of life,⁹ increased risk of hospitalization¹⁰ and functional disability¹¹ and worse treatment outcomes.¹²

As a result of pharmacokinetic changes in older adults that alter the absorption, metabolism and excretion of drugs,¹³ older people are more prone to drug-induced adverse events.¹⁴ Therefore, prescription of antidepressants in older adults, particularly those with physical comorbidities, should be done with caution.¹⁵ Surveys of prescription patterns are an efficient approach to appraise the appropriateness of psychopharmacotherapy.¹⁶ It is, therefore, important to investigate the patterns of use of antidepressants in older adults with physical comorbidities.

This study examined the patterns of physical comorbidities and their associated demographic and clinical factors in older psychiatric patients

prescribed with antidepressants in Asia. We hypothesized that physical comorbidities in older patients prescribed with antidepressants are common and independently associated with clinical risk factors.

METHODS

Study design and sample

The Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) project is a pharmaco-epidemiological survey of the antidepressant prescription patterns in psychiatric patients across 42 psychiatric centers in 10 Asian countries/regions (China, Singapore, Hong Kong, Japan, Korea, Taiwan, India, Malaysia, Thailand and Indonesia). All patients treated with antidepressants on the day of the survey were enrolled without any exclusion criteria. Data were collected using a standardized protocol and procedure at all study sites.

The current study is a secondary analysis of the database of the REAP-AD 2013 that was conducted between March and June 2013. Data of all patients who were ≥ 50 years old were analyzed. In most Asian countries, patients aged ≥ 50 years were defined as 'older adults' in the REAP-AD project. This cut-off age is in line with other studies.¹⁷⁻¹⁹

For logistical reasons, the presence of 10 core depressive symptoms selected from the National Institute for Health and Care Excellence (NICE) guidelines, ICD-10²⁰ and DSM-IV²¹ that included insomnia, appetite change, agitation, fatigue, suicidal ideation, guilt/self-blame, lack of confidence, poor concentration, sadness and loss of interests²² were recorded. The participating countries and territories were collapsed into high income (Hong Kong, Singapore, Japan, Korea, and Taiwan) and middle income sites (China, Malaysia, Thailand, India and Indonesia) according to the World Bank criteria (<https://datahelpdesk.worldbank.org/knowledgebase/articles/906519>).

Data collection

Demographic and clinical characteristics including physical comorbidities were collected either by a review of medical records only, or a review of medical records review that was supplemented by a clinical interview by the patients' attending psychiatrists or by members of the research team. Principal

psychiatric diagnoses were made according to the International Classification of Diseases, 10th Revision²⁰ or the Diagnostic and Statistical Manual of Mental Disorders, 4th edition.²¹ Psychotropic medications were categorized according to the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system. In this study, physical comorbidities included myocardial infarction, congestive heart failure, cerebrovascular diseases, peripheral vascular diseases, dementia, peptic ulcer, liver diseases, chronic pulmonary diseases, diabetes mellitus, renal diseases, rheumatic diseases, acquired immunodeficiency syndrome/human immunodeficiency virus, malignancy, and other specified diseases.

The research and ethics committee at each study site approved the research protocol. When the study involved anonymous retrospective medical chart review, informed consent was waived at the study sites because it was considered low risk to patients. When patients were interviewed, they provided written informed consent.

Data analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 22.0 (IBM SPSS, Chicago, IL, USA). Group differences were compared between older adults with physical comorbidities and those without using chi-squared test, independent sample *t*-test and Mann-Whitney *U*-test, as appropriate. Multiple logistic regression analysis with the 'Enter' method (i.e. all independent variables were entered into the model simultaneously) was carried out to identify the independent associations with physical comorbidities. Presence of physical comorbidities was the dependent variable, whereas those that significantly differed between the two groups in univariate analyses were the independent variables. Level of significance was set at 0.05 (two-tailed).

RESULTS

Of the 955 older adults included in the analyses, 421 (44%) had at least one physical comorbidity (Table 1). The most common physical comorbidity was diabetes, followed by cerebrovascular diseases, peptic ulcer, malignancy and peripheral vascular diseases (Table 2).

Table 1 Distribution of patients with physical comorbidities across Asian countries/territories

Country/territory	Patients <i>n</i> = 955	Physical comorbidities	
		<i>n</i> = 421	%
China	158	41	9.7
Hong Kong	39	17	4.0
Japan	119	73	17.3
South Korea	150	68	16.2
Singapore	48	26	6.2
Taiwan	109	56	13.3
India	63	26	6.2
Malaysia	67	41	9.7
Thailand	128	44	10.5
Indonesia	74	29	6.9
Overall	955	421	44.0

Table 2 Most common physical comorbidities in patients treated with antidepressants in Asia (*n* = 421)

Primary physical comorbidity	<i>N</i>	%
Diabetes mellitus	116	27.5
Cerebrovascular diseases	48	11.4
Peptic ulcer	24	5.7
Malignancies	24	5.7
Peripheral vascular diseases	21	4.9

Basic demographic and clinical characteristics of the whole sample and separately by physical comorbidities are shown in Table 3. Older age, high number of depressive symptoms, being treated in psychiatric hospital, living in high-income countries/territories, use of benzodiazepines (BZD), use of noradrenergic and specific serotonergic antidepressants (NaSSA) and diagnosis of 'other psychiatric disorders' were significantly associated with physical comorbidities. Patients in higher income countries/territories were older than those in middle income countries/territories (63.6 ± 9.9 vs. 61.5 ± 9.0 years, $P < 0.05$). Multiple logistic regression analysis showed that older age, high number of depressive symptoms, being treated in psychiatric hospital, living in high-income countries/territories, use of BZD and diagnosis of 'other psychiatric disorders' were independently and significantly associated with physical comorbidities (Table 4).

DISCUSSION

To the best of our knowledge, this was the first large-scale, international survey of the patterns of physical comorbidities in older psychiatric patients

Table 3 Basic demographic and clinical characteristics of patients with and without physical comorbidities

	Total sample (n = 955)		No physical comorbidities (n = 534)		Physical comorbidities (n = 421)		Statistics		
	Mean	SD	Mean	SD	Mean	SD	t/z	df	P-value
Age (years)	62.6	9.5	61.0	8.8	64.5	10.0	-5.6	953	<0.001***
AD dose, IMI-eq (mg/d)	131.2	112.5	132.1	119.2	129.9	103.4	-0.3	-†	0.73
No. of antidepressants	1.2	0.5	1.2	0.4	1.2	0.5	-0.08	-†	0.93
No. of depressive symptoms	3.4	2.0	3.3	2.0	3.6	2.0	-2.1	-†	0.03*
	N	%	N	%	N	%	χ^2	df	P-value
Age (years)							22.8	1	<0.001***
50–64	615	64.4	379	71.0	236	56.1			
65 and older	340	35.6	155	29.0	185	43.9			
Female	580	60.7	333	62.4	247	58.7	1.3	1	0.24
Psychiatric hospital patients	351	36.8	234	43.8	117	27.8	26.0	1	<0.001***
Inpatients	233	24.4	125	23.4	108	25.7	0.6	1	0.42
Public hospital patients	687	71.9	388	72.7	299	71.0	0.3	1	0.57
Income group							20.8	1	<0.001***
High income	465	48.7	225	42.1	240	57.0			
Middle income	490	51.3	309	57.9	181	43.0			
Use of FGA	83	8.7	48	9.0	35	8.3	0.1	1	0.71
Use of SGA	238	24.9	127	23.8	111	26.4	0.8	1	0.36
Use of MS	63	6.6	33	6.2	30	7.1	0.3	1	0.55
Use of BZD	423	44.3	215	40.3	208	49.4	7.9	1	0.005**
Principal psychiatric diagnosis							14.9	3	0.002**
Mood disorders	671	70.3	386	72.3	285	67.7			
Anxiety disorders	130	13.6	76	14.2	54	12.8			
Schizophrenia	79	8.3	46	8.6	33	7.8			
Others	75	7.9	26	4.9	49	11.6			
Use of antidepressants									
TCA	99	10.4	60	11.2	39	9.3	0.9	1	0.32
Tetracyclic	27	2.8	18	3.4	9	2.1	1.3	1	0.25
SSRI	593	62.1	336	62.9	257	61.0	0.3	1	0.55
SNRI	155	16.2	85	15.9	70	16.6	0.08	1	0.76
NaSSA [‡]	163	17.1	78	14.6	85	20.2	5.1	1	0.023*
Others	127	13.3	71	13.3	56	13.3	0	1	0.99

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. † Mann-Whitney *U*-test. ‡ NaSSA were available in all countries/territories except Indonesia. Bolded values, < 0.05 . AD, antidepressant; BZD, benzodiazepine; FGA, first-generation antipsychotic; IMI-eq, imipramine-equivalent; MS, mood stabiliser; NaSSA, noradrenergic and specific serotonergic antidepressant; SGA, second-generation antipsychotic; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant. –, not applicable.

Table 4 Independent demographic and clinical correlates in patients with physical comorbidities

Variables	P-value	Odds ratio	95% CI
65 years and older	<0.001***	1.7	1.3–2.3
Psychiatric hospital patients	0.002**	0.5	0.4–0.8
High-income group	0.002**	2.4	1.3–4.2
Principal psychiatric diagnosis			
Mood disorders	–	1	–
Anxiety disorders	0.97	1.008	0.6–1.5
Schizophrenia	0.78	1.07	0.6–1.8
Others	<0.001***	2.7	1.5–4.6
No. of depressive symptoms [†]	0.016*	1.09	1.01–1.1
On NaSSA	0.41	1.1	0.8–1.6
On BZD	0.013*	1.4	1.08–1.9

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. † As a result of collinearity between the number of core depressive symptoms and the individual core depressive symptom, the individual core depressive symptom cannot be entered as an independent variable. Bolded values, < 0.05 ; participating country/territory has been controlled for as a covariate. Multiple logistic regression analysis with diagnosis of mood disorders as the reference group. BZD, benzodiazepine; NaSSA, noradrenergic and specific serotonergic antidepressant. –, not applicable.

prescribed with antidepressants. In the present study, 44% of older psychiatric patients prescribed with antidepressants had at least one physical comorbidity. Given that we could not locate similar studies of this kind, no direct comparisons could be made with previous studies. In a study examining the use of electroconvulsive therapy in older psychiatric patients, the proportion of physical comorbidities was 68.6% (1604/2339),²² which is higher than our results. The cut-off age for older patients in this study, however, was older (60 vs. 50 years), which could partly explain the differing frequency of physical comorbidities between the two studies.

Previous studies have found that the increased use of antidepressants in older adults was mainly driven by the introduction of selective serotonin

reuptake inhibitors (SSRI).⁷ This was partly supported by our study that 62.1% of the whole sample received SSRI. Apart from depressive symptoms, sleep disturbances and anxiety symptoms are also common in older adults. SSRI are effective at relieving anxiety and anxiety-related insomnia with relatively few adverse events and good treatment adherence,²³ which could also increase their use.

As benzodiazepines are also commonly used for anxiety and sleep disturbances,^{24,25} they are frequently used in older patients with physical diseases.²⁶ Similarly, this study found that physical comorbidities could increase the likelihood and severity of depressive symptoms.^{27,28} As expected, in this study, older age was associated with higher risk of physical comorbidities; therefore, patients with physical comorbidities were more likely to receive treatment in hospital settings.

In this multi-site study, older patients living in high-income countries/territories were more likely to have physical comorbidities. Compared to middle-income countries/territories, hospitals in high-income countries/territories usually have higher staff–patient ratio and better medical equipment and training; therefore, regular screening tests for physical diseases are more frequent. In addition, psychiatric patients in middle-income countries/territories are more likely to be treated in psychiatric institutions in which general medical services are not easily accessible. As a result, physical comorbidities in psychiatric patients treated in high-income countries/territories are more likely to be identified. As expected, patients with physical comorbidities were less likely to be treated in psychiatric hospitals because general hospitals usually had better medical equipment and training in treating physical diseases.

Older patients with major psychiatric disorders use medical health services frequently as a result of physical diseases.¹¹ However, in this study, patients with other psychiatric disorders were more likely to have physical comorbidities; 65.3% of other psychiatric disorders were organic mental disorders and 18.6% were substance abuse disorders. This may explain why these patients had more physical comorbidities.

Strengths of the present study include its large sample size and the representative samples across Asia. However, there are several

limitations. First, as a result of logistical reasons, the presence of physical comorbidities could not be confirmed by direct medical examination or investigations. Second, depressive symptoms were not assessed with standardized tools. Third, there was no control group. Finally, as a result of the cross-sectional design, causality between physical comorbidities and other variables could not be examined.

In conclusion, nearly half of older adults treated with antidepressants in this cohort had physical comorbidities. Considering the high prevalence of physical comorbidities, integrating physical care into the treatment of older psychiatric patients should urgently be considered.

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