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Physical comorbidities in older adults prescribed with antidepressants in Asia

Running Head: Physical comorbidities in older adults

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ABSTRACT:

Background: This 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: The proportion of physical comorbidities in this cohort was 44%. Multiple logistic regression analyses revealed that older age (OR=1.7, $P < 0.001$), high number of depressive symptoms (OR=1.09, $P = 0.016$), being treated in psychiatric inpatient units (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 older adult population. In Europe, 47% older adults experienced at least one psychiatric disorder in their life-time, and nearly one fourth had a current psychiatric disorder.² The 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 due to 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

Due to 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, thus, 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

For logistical reasons, the presence of 10 core depressive symptoms selected from the National Institute for Health and Care Excellence (NICE) guidelines, ICD-10 ¹⁸ and DSM-IV ¹⁹ that included insomnia, appetite change, agitation, fatigue, suicidal ideation, guilt/self-blame, lack of confidence, poor concentration, sadness and loss of interests ²⁰ 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 Revision ²¹ or Diagnostic and the Statistical Manual of Mental Disorders, 4th edition. ¹⁹ Psychotropic medications were categorized according to the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system ²². 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.²³

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-square 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 performed to identify the independent associations with physical comorbidities. The presence of physical comorbidities was the dependent variable, while those that significantly differed between the two groups in univariate analyses were the independent variables. The level of significance was set at 0.05 (two-tailed).

RESULTS

Of the 954 older adults included in the analyses, 421 (44%) had at least 1 physical comorbidity (Table 1). The most common physical comorbidity was diabetes, followed by cerebrovascular diseases, peptic ulcer, malignancy and peripheral vascular diseases (Table 2).

The basic demographic and clinical characteristics of the whole sample and

separately by physical comorbidities are showed in Table 3. Older age, high number of depressive symptoms, being treated in general hospital psychiatric units, living in high income countries/territories, use of benzodiazepines (BZD), use of noradrenergic and specific serotonergic antidepressants (NaSSAs) and diagnosis of 'other psychiatric disorders' were significantly associated with physical comorbidities. Patients in higher income countries/territories were older than in middle income countries/territories (63.6 ± 9.9 vs. 61.5 ± 9.0 years, $p < 0.05$). Multiple logistic regression analysis revealed that older age, high number of depressive symptoms, being treated in general hospital psychiatric units, 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 prescribed with antidepressants. In this 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 use of electroconvulsive therapy in older

psychiatric patients the proportion of physical comorbidities was 66.9% (1,604/2,339),²⁴ 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 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 (SSRIs).⁷ This notion was partly supported by our study in that 62.1% of the whole sample received SSRIs. Apart from depressive symptoms, sleep disturbances and anxiety symptoms are also common in older adults. SSRIs are effective to relieve anxiety and anxiety-related insomnia with relatively few adverse events and good treatment adherence,²⁵ which could also increase their use.

As benzodiazepines are also used commonly for anxiety and sleep disturbances,²⁶ they are frequently used in older patients with physical diseases.²⁷ Similarly, this study found that physical comorbidities could increase the likelihood and severity of depressive symptoms.²⁸ As expected, older age was associated with higher risk of physical comorbidities in this study 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.

Older patients with major psychiatric disorders utilize medical health services frequently due to physical diseases.²⁹ However, in this study patients with other psychiatric disorders were more likely to have physical co-morbidities; 65.3% of other psychiatric disorders were organic mental disorders and 18.6% substance abuse disorders. This may explain why these patients had more physical co-morbidities.

The strengths of this study include its large sample size and the representative samples across Asia. However, there are several limitations. First, due to 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, due to 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 co-morbidities. Considering the high prevalence of physical comorbidities, integrating physical care into the treatment of older psychiatric patients should be urgently considered.

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Disclosure statement

We declare that the authors have no competing interests related to this study.

REFERENCE

1. Commission of the European Communities. Confronting demographic change: a new solidarity between generations, Green Paper, Brussels, 16 March 2005.
2. Andreas S, Schulz H, Volkert J, et al. Prevalence of mental disorders in elderly people: the European MentDis_ICF65+ study. *Br J Psychiatry* 2017; **210**: 125-131.
3. Ford BC, Bullard KM, Taylor RJ, Toler AK, Neighbors HW, Jackson JS. Lifetime and 12-month prevalence of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition disorders among older African Americans: findings from the National Survey of American Life. *Am J Geriatr Psychiatry* 2007; **15**: 652-659.
4. McCarthy M. Antidepressant use has doubled in rich nations in past 10 years. *BMJ* 2013; **347**: f7261.
5. Toumi DMNB-ESJJZM. Growth in Antidepressant Use in 10 Countries in the Last Decade. *Value in Health* 2012; **15**: A93-A94.
6. Moore M, Yuen HM, Dunn N, Mullee MA, Maskell J, Kendrick T. Explaining the rise in antidepressant prescribing: a descriptive study using the general practice research database. *BMJ* 2009; **339**: b3999.
7. Sonnenberg CM, Deeg DJ, Comijs HC, van Tilburg W, Beekman AT. Trends in

antidepressant use in the older population: results from the LASA-study over a period of 10 years. *J Affect Disord* 2008; **111**: 299-305.

8. Hendrie HC, Lindgren D, Hay DP, et al. Comorbidity profile and healthcare utilization in elderly patients with serious mental illnesses. *Am J Geriatr Psychiatry* 2013; **21**: 1267-1276.

9. Fenn HH, Bauer MS, Altshuler L, et al. Medical comorbidity and health-related quality of life in bipolar disorder across the adult age span. *J Affect Disord* 2005; **86**: 47-60.

10. Ho C, Feng L, Fam J, Mahendran R, Kua EH, Ng TP. Coexisting medical comorbidity and depression: multiplicative effects on health outcomes in older adults. *Int Psychogeriatr* 2014; **26**: 1221-1229.

11. Rej S, Yu C, Shulman K, et al. Medical comorbidity, acute medical care use in late-life bipolar disorder: a comparison of lithium, valproate, and other pharmacotherapies. *Gen Hosp Psychiatry* 2015; **37**: 528-532.

12. Kemp DE, Gao K, Chan PK, Ganocy SJ, Findling RL, Calabrese JR. Medical comorbidity in bipolar disorder: relationship between illnesses of the endocrine/metabolic system and treatment outcome. *Bipolar disorders* 2010; **12**: 404-413.

13. Oslin DW, Datto CJ, Kallan MJ, Katz IR, Edell WS, TenHave T. Association between medical comorbidity and treatment outcomes in late-life depression. *J*

Am Geriatr Soc 2002; **50**: 823-828.

14. Masand PS. Side effects of antipsychotics in the elderly. *J Clin Psychiatry* 2000; **61 Suppl 8**: 43-49.

15. Meyers BS, Jeste DV. Geriatric psychopharmacology: evolution of a discipline. *J Clin Psychiatry* 2010; **71**: 1416-1424.

16. Manthey L, van Veen T, Giltay EJ, et al. Correlates of (inappropriate) benzodiazepine use: the Netherlands Study of Depression and Anxiety (NESDA). *Br J Clin Pharmacol* 2011; **71**: 263-272.

17. Ungvari GS, Chow LY, Chiu HF, Ng FS, Leung T. Modifying psychotropic drug prescription patterns: a follow-up survey. *Psychiatry Clin Neurosci* 1997; **51**: 309-314.

18. Dassori AM, Copeland LA, Zeber JE, Miller AL. Factors in second-generation antipsychotic switching patterns in a national sample of older veterans with schizophrenia. *Psychiatr Serv* 2011; **62**: 47-53.

19. Xiang YT, Li Y, Correll CU, et al. Common use of high doses of antipsychotic medications in older Asian patients with schizophrenia (2001-2009). *Int J Geriatr Psychiatry* 2014; **29**: 359-366.

20. WHO. Information Needs for Research, Policy and Action on Ageing and Older Adults. 2001.

21. World Health Organisation. ICD-10 Classifications of Mental and Behavioural

- Disorder: Clinical Descriptions and Diagnostic Guidelines. Geneva, WHO,1992.
- 22.APA. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington: American Psychiatric Association; 1994.
- 23.Chee KY, Tripathi A, Avasthi A, et al. International study on antidepressant prescription pattern at 40 major psychiatric institutions and hospitals in Asia: A 10-year comparison study. *Asia Pac Psychiatry* 2015; **7**: 366-374.
- 24.Chee KY, Tripathi A, Avasthi A, et al. Country variations in depressive symptoms profile in Asian countries: Findings of the Research on Asia Psychotropic Prescription (REAP) studies. *Asia Pac Psychiatry* 2015; **7**: 276-285.
- 25.Shinfuku N, Tan CH. Pharmacotherapy for schizophrenic inpatients in East Asia--changes and challenges. *Int Rev Psychiatry* 2008; **20**: 460-468.
- 26.Zhang XQ, Wang ZM, Pan YL, et al. Use of electroconvulsive therapy in older Chinese psychiatric patients. *Int J Geriatr Psychiatry* 2015; **30**: 851-856.
- 27.Kunik HFSKUBM. Anxiety and Depression in Medically Ill Older Adults. *Journal of Clinical Geropsychology* 2001; **7**: 117-130.
- 28.Tor PC, Ng TP, Yong KH, et al. Adjunctive benzodiazepine treatment of hospitalized schizophrenia patients in Asia from 2001 to 2008. *Int J Neuropsychopharmacol* 2011; **14**: 735-745.
- 29.Xiang YT, Weng YZ, Leung CM, Tang WK, Ungvari GS. Clinical and social

determinants of long-term use of benzodiazepines and its impact on quality of life of Chinese schizophrenia patients. *Pharmacopsychiatry* 2007; **40**: 269-274.

30. Luijendijk HJ, Tiemeier H, Hofman A, Heeringa J, Stricker BH. Determinants of chronic benzodiazepine use in the elderly: a longitudinal study. *Br J Clin Pharmacol* 2008; **65**: 593-599.

31. Shi YZ, Xiang YT, Yang Y, et al. Depression after minor stroke: the association with disability and quality of life - a 1-year follow-up study. *Int J Geriatr Psychiatry* 2016; **31**: 421-427.

32. Wong TS, Xiang YT, Tsoh J, et al. Depressive disorders in older patients with chronic obstructive pulmonary disease (COPD) in Hong Kong: a controlled study. *Aging Ment Health* 2014; **18**: 588-592.

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

Country/territory	Patients	Physical comorbidities	
		n=421	%
China	158	41	9.7
Hong Kong	39	17	4.0
Japan	119	73	17.3
RO 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	N	%
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

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	<i>t/z</i>	<i>df</i>	<i>P</i>
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	-- ^a	0.73
Number of antidepressants	1.2	0.5	1.2	0.4	1.2	0.5	-0.08	-- ^a	0.93
Number of depressive symptoms	3.4	2.0	3.3	2.0	3.6	2.0	-2.1	-- ^a	0.03
	N	%	N	%	N	%	χ^2	<i>df</i>	<i>P</i>
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	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
General hospital	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 ^b	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
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Bolded values: <0.05; a: Mann–Whitney U-test; b: NaSSAs were available in all countries/territories except Indonesia; AD=antidepressants; IMI-eq=imipramine-equivalent; FGA= first-generation antipsychotic; SGA=second-generation antipsychotic; MS=mood stabilizer; BZD=benzodiazepines; TCA=tricyclic antidepressants; SSRI=selective serotonin reuptake inhibitors; SNRI=serotonin-norepinephrine reuptake inhibitors; NaSSA= noradrenergic and specific serotonergic antidepressant.

TABLE 4. Independent demographic and clinical correlates in patients with physical comorbidities

Variables	<i>P</i> value	Odds Ratio	95% CI
65 years and older	<0.001	1.7	1.3-2.3
Psychiatric hospital	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
Number of depressive symptoms ^a	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

Bolded values: <0.05; a: due to collinearity between the number of core depressive symptoms and the individual core depressive symptom, the individual core depressive symptom cannot be entered as independent variable. Participating country/territory has been controlled for as a covariate. Multiple logistic regression analysis with diagnosis of mood disorders as the reference group. NaSSA=noradrenergic and specific serotonergic antidepressant; BZD=benzodiazepines