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A comparison of clinical characteristics of older adults treated with antidepressants between general and psychiatric hospitals in Asia

Running head: Use of antidepressants in Asia

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ABSTRACT

Introduction This study compared the demographic, clinical characteristics and antidepressant prescription pattern between Asian patients aged 50 years and older attending psychiatric and general hospitals.

Method A total of 955 patients (604 in general hospitals and 351 in psychiatric hospitals) aged 50 years or older treated with antidepressants in 10 Asian countries and territories were examined. Patients' demographic and clinical features and prescriptions of psychotropic drugs were recorded using a standardized protocol and data collection procedure.

Results Binary logistic regression revealed that high income and diagnosis of schizophrenia were independently associated with psychiatric hospital treatment, while outpatient care, diagnosis of anxiety disorders and multiple major medical conditions were independently associated with general hospital treatment. In addition, tetracyclic and noradrenergic and specific serotonergic antidepressant (NaSSA) were more likely to be prescribed in general hospitals, whereas second-generation antipsychotics were more likely to be prescribed in psychiatric hospitals.

Conclusion Older adults treated with antidepressants showed different demographic and clinical features between general hospitals and psychiatric hospitals in Asia.

Key words: antidepressants, prescription patterns, Asia

INTRODUCTION

Due to the low birth rate and the increase in life expectancy, the proportion of the aging population in many Asian countries has been rapidly increasing.[1] As a consequence, health issues in this population have attracted much attention.[2] Depressive disorders, such as major depression and dysthymia, are common in the elderly with negative outcomes including functional disability, increased mortality and high utilization of health care services and costs.[3,4]

During the past decades, antidepressants was among the most widely prescribed medications in many countries.[5-8] The reasons for increased use of antidepressants include the introduction of many new and safe antidepressants and broad range of indications for their use.[9,10] For example, apart from depression, selective serotonin reuptake inhibitors (SSRIs) have also been used for alcoholism, eating and anxiety disorders.[11,12]

In Asian countries standalone psychiatric hospitals and general hospitals are the two major mental health service providers. Patients treated in different clinical settings usually have different demographic and clinical features including prescription patterns of psychotropic medications. For example, in China psychiatric hospital are mainly located in suburban areas and provide intensive services for severe psychiatric disorders , while general hospital are located in cities.[13] In China, it has been reported that 73% of antidepressants are

prescribed in general hospital settings.[14] To date, no study has examined the demographic and clinical features of older Asian adults attending psychiatric and general hospitals.

Regular surveys on prescription patterns in psychiatry are an efficient way of identifying the use and trend of specific treatments over time in a given clinical setting. [15,16] A large-scale longitudinal, observational project entitled the Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) was initiated in 2003. The first and second REAP-AD surveys were conducted in November, 2003 and between March and June, 2013, respectively employing the same research design and protocol. [17,18]

In order to provide a better understanding and improve the rationale of antidepressant utilization in older Asian adults, we conducted a secondary analysis of the data in the 2013 REAP-AD survey that sought to (1) compare the demographic and clinical features of Asian patients aged 50 years and older treated with antidepressants at both general and psychiatric hospitals, and (2) identify the independent correlates of antidepressant treatment between these two treatment settings. Considering that antidepressants are psychiatric medications, we hypothesized that there would be more patients receiving antidepressants in psychiatric hospitals than in general hospitals.

METHOD

Study sample and sites

The second REAP-AD survey was conducted in 40 psychiatric hospitals/units in the following Asian countries and territories: mainland China (China thereafter), Hong Kong, Taiwan, India, Indonesia, Japan, Korea, Malaysia, Singapore, and Thailand. A consensus meeting was held to agree upon the procedures of case selection, data collection and data entry procedures. The same standardized protocol and data collection procedure were used in all the participating centers. Patients were included if they (1) were in- or outpatients; (2) aged 50 years or above. The age cutoff for older adults varied from 50 to 65 years across the participating institutions according to local cultural and professional traditions. In order to make the population homogeneous, those aged 50 years and older in the dataset of the REAP-AD project were defined as 'older adults' in this study. The same age cutoff was also used in WHO reports and other recent studies;[19-22] (3) received antidepressants on the day of the survey; (4) were able to comprehend the aims of the study and provide informed consent if interviewed. There were no exclusion criteria.

Procedures

All eligible patients were recruited consecutively at each site. Basic demographic

and clinical characteristics including the type of clinical setting, age, gender, financial category, principal ICD-10 psychiatric diagnosis, depressive symptoms and medical treatment were collected using a data collection form designed for the study. Due to logistic limitations, no standardized instruments on presence and severity of depressive symptoms were used. Instead, the presence of 10 core depressive symptoms selected from the National Institute for Health and Care Excellence (NICE) guidelines, ICD-10[23] and DSM-IV[24] were used including insomnia, appetite change, agitation, fatigue, suicidal ideation, guilt/self-blame, lack of confidence, low concentration, sadness and loss of interests.[25] In addition, all the participating countries and territories were divided into high income (Hong Kong, Singapore, Japan, Korea, and Taiwan), upper middle income (China, Malaysia, and Thailand), and lower middle income sites (India and Indonesia) according to the World Bank criteria. The above data were collected by either a review of medical records only or a medical review supplemented by a clinical interview. Data were collected by the patients' attending psychiatrists or by members of the research team with the agreement of the psychiatrists in charge of the patients.

Classification of prescribed medication

The prescribed medications were classified into antidepressants, first generation

antipsychotics (FGAs), second generation antipsychotics (SGAs), mood stabilizers and benzodiazepines according to the Anatomical Therapeutic Chemical classification (ATC).[26] In this survey, SGAs included aripiprazole, amisulpride, blonanserin, clozapine, olanzapine, paliperidone, perospirone, quetiapine, risperidone, ziprasidone and zotepine. Antidepressants included escitalopram, mirtazapine, sertraline, trazodone, paroxetine, fluoxetine, duloxetine, fluvoxamine, venlafaxine, amitriptyline, citalopram, imipramine, bupropion, clomipramine, mianserin, agomelatine, dothiepin, doxepin, milnacipran, maprotiline, nortriptyline and tandospirone. Antidepressants were classified into 7 classes: tricyclic (TCAs), tetracyclic, monoamine oxidase inhibitors (MAOIs), SSRIs, serotonin norepinephrine reuptake inhibitors (SNRIs), noradrenergic and specific serotonergic antidepressant (NaSSA) and other antidepressants.

The study was approved by the clinical research ethics committees of the respective institutions. Given the anonymous nature of the retrospective chart review for the purpose of a clinical audit, informed consent was not required at some study sites in line with local ethical standards, provided that only the medical records were reviewed. All patients who were interviewed gave written consent according to the requirements of the respective clinical research ethics committees.

Data analysis

All analyses were performed using the Statistical Package for Social Science (SPSS) version 20.0. Comparisons between patients' socio-demographic and clinical characteristics treated with antidepressants in general and psychiatric hospitals were performed by independent sample t-test, Mann-Whitney U test and Chi-square test, as appropriate. Binary logistic regression analyses with the "enter" method were used to identify independent demographic and clinical correlates of the two types of treatment settings. The variables that were statistically significant in the above univariate analysis were entered as independent variables, while the treatment setting was the dependent variable. The significance level was set at 0.05 (two-tailed).

RESULTS

Altogether 955 patients from the REAP-AD database fulfilled the study criteria; 604 (63.2%) received treatment in general hospitals and 351 (36.8%) in psychiatric hospitals. Table 1 presents the socio-demographic and clinical characteristics of patients by study site. Table 2 shows the socio-demographic and clinical characteristics of the whole sample and separately by treatment settings. Compared to general hospitals, patients treated at psychiatric hospital

were younger, more likely to be male, inpatients and diagnosed with schizophrenia, had lower income, less major medical conditions and were less likely to receive tetracyclic and NaSSA antidepressants, but more likely to receive antipsychotics.

Table 3 shows that outpatients, having anxiety disorders and more major medical conditions were independently associated with less frequent treatment in psychiatric hospitals, while falling into upper middle financial category and having schizophrenia were associated with more frequent treatment in psychiatric hospitals. In addition, tetracyclic antidepressants and NaSSA were more likely to be prescribed in general hospitals.

DISCUSSION

This was the first large-scale, multicenter survey comparing clinical characteristics of older adults treated with antidepressants between general and psychiatric hospitals in Asia. Around two third of the whole sample received antidepressants in general hospitals, consistent with a previous finding (73%) in adult patients with mood disorders in China.[14] The results do not support our hypothesis that there would be more patients receiving antidepressants in psychiatric hospitals than in general hospitals. Before the introduction of SSRIs, traditional antidepressants, particularly TCAs and MAOIs, had been prescribed cautiously due to their cardiotoxicity and high lethality in overdose. In the past decades, however, the use of antidepressants have increased rapidly in all age groups in both psychiatric and other clinical settings since SSRIs and other novel antidepressants are more tolerable and safe. Apart from the broad range of indications of novel antidepressants,[9,10] off-label use and overuse of antidepressants could contribute to the increasing use.[27] Off-label use and overuse of antidepressants are associated with a number of negative outcomes, such as increased treatment costs and increased risk of adverse events, withdrawal reactions and even suicide. [28,29]

There were significant demographic and clinical differences between the two treatment settings across Asia. Surprisingly, on average only around three

depressive symptoms were reported by this sample receiving antidepressants, which may be possibly due to the wide indications of antidepressants. For example, patients with anxiety or eating disorders were usually prescribed antidepressants. [11,12] The most frequent diagnosis in this survey was mood disorder (70.3%) followed by anxiety disorders (13.6%), schizophrenia (8.3%) and other psychiatric disorders. The benefit and risk ratio associated with the common use of antidepressants still needs to be clarified. Although compelling evidence for the usefulness of antidepressants in schizophrenia is not available, [30,31] a significant proportion of patients treated with antidepressants in this sample had a diagnosis of schizophrenia. Antidepressants are also not recommended for maintenance treatment of bipolar I disorder as they may increase the risk of rapid cycling, [32] more severe symptoms and impaired psychosocial functioning. [33] Subtype of mood disorders including bipolar I disorder however could not be identified in this sample because only the main ICD-10 codes were used in the REAP surveys.

Different health service models may help explain the relationship between patients' characteristics and the type of hospitals found in this study. Penchansky and Thomas described the 5 ''A's'' of access to health care: affordability, acceptability, accommodation, accessibility and availability to explain the overall relationships between patients and providers. [34,35] Another model concerning the

use of mental health services has four interacting components (1) patients' demographic and clinical features, (2) patient' social support system, (3) illness career comprising factors such as sick role, recovery, compliance, and spacing of consultations; and (4) the treatment system. [36-38] In this study schizophrenia patients were more likely to be treated in psychiatric hospitals. This is consistent with a finding that the percentage of schizophrenia patients in psychiatric hospitals is higher than that in general hospitals. [39] Similar to another study, [40] financial factors may have an important role in selection of health service and treatment in this study. Many Asian psychiatric hospitals largely treat patients with severe mental illness and are located in suburban areas, while general hospital psychiatric units are usually located in cities and provide outpatient services for patients with less severe mood and anxiety disorders. [13,14] This likely explains the negative associations between psychiatric hospital treatment and outpatient care with the diagnosis of anxiety and depressive disorders. Patients with both psychiatric and medical co-morbidities need easy access to medical treatment, thus are more likely receive treatment in general hospitals as found in this study.

Psychiatric hospital patients received less frequently tetracyclic antidepressants and NaSSA, which has no clear explanation. A number of socio-cultural and economic factors, clinical traditions, psychotropic drugs

availability, cost and insurance coverage, and health care policy might all contribute to the variations of antidepressant prescribing practice across Asian countries.

There are several limitations to this study. First, several relevant variables, such as health care policies, availability and cost of drugs, psychiatric training, treatment guidelines, prior treatment history, reasons for antidepressant prescriptions and treatment responses, were not recorded in the REAP-AD survey. Second, due to the cross-sectional design, the causal relationships between variables cannot be examined. Finally, due to logistic reasons, the presence of depressive symptoms was not measured using standardized instruments. However, the strengths of this study include the relatively large sample size, the diversity of the sample across ten Asian countries and the standardized nature of the data collection.

In conclusions, this REAP-AD survey found that majority of the whole sample received antidepressants in general hospitals and there is considerable variation in demographic and clinical characteristics in Asian old adults receiving antidepressants between psychiatric and general hospitals. The appropriateness of antidepressant prescription in general hospitals needs to be examined. The findings will help clinicians to better understand and rationalize the prescription patterns of antidepressants and the provision of different types of mental health

services across Asia.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest related to this study.

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Table 1. Socio-demographic and clinical characteristics of the sample

	China (n=158)		Hong Kong (n=39)		Japan (n=119)		Korea (n=150)		Singapore (n=48)		Taiwan (n=109)		India (n=63)		Malaysia (n=67)		Thailand (n=128)		Indonesia (n=74)	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age (yrs)	61.89	8.37	57.9	7.46	65.71	9.4	64.61	9.37	61	9.46	63.45	11.18	60.73	8.66	61.87	9.72	63.21	10.26	58.43	7.19
No. of depressive symptoms	4.18	2.29	2.15	1.5	3.7	1.88	3.88	1.85	3.63	2.48	3.36	1.61	3.63	2.52	4.49	2.17	2.59	1.57	2.01	1.29
No. of major medical conditions	0.32	0.62	0.49	0.60	1.06	1.20	0.56	0.7	0.75	0.81	0.7	0.81	0.49	0.64	0.87	0.94	0.41	0.62	0.49	0.69
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Male gender	54	34.2	10	25.6	52	43.7	42	28	24	50	55	50.5	34	54	25	37.3	52	40.6	27	36.5
Outpatient care	84	53.2	28	71.8	76	63.9	135	90	35	72.9	75	68.8	60	95.2	61	91	109	85.2	59	79.7
Financial category																				
High	0	0	39	100	119	100	150	100	48	100	109	100	0	0	0	0	0	0	0	0
Upper middle	158	100	0	0	0	0	0	0	0	0	0	0	0	0	67	100	128	100	0	0
Lower middle	0	0	0	0	0	0	0	0	0	0	0	0	63	100	0	0	0	0	74	100
Principal psychiatric diagnosis																				
Mood disorders	137	86.7	23	59	93	78.2	117	78	24	50	67	61.5	44	69.8	50	74.6	81	63.3	35	47.3
Anxiety	17	10.8	8	20.5	14	11.8	11	7.3	11	22.9	4	3.7	17	27	6	9	19	14.8	23	31.1
Schizophrenia	0	0	6	15.4	2	1.7	7	4.7	11	22.9	28	25.7	1	1.6	7	10.4	7	5.5	10	13.5
Others	4	2.5	2	5.1	10	8.4	15	10	2	4.2	10	9.2	1	1.6	4	6	21	16.4	6	8.1
SGAs	48	30.4	11	28.2	31	26.1	28	18.7	14	29.2	41	37.6	12	19	14	20.9	19	14.8	20	27
FGAs	5	5.3	6	15.4	11	9.2	8	5.3	4	8.3	10	9.2	6	9.5	6	9	12	9.4	15	20.3
Mood stabilizers	44	27.8	4	10.3	20	16.8	12	8	6	12.5	31	28.4	29	46	12	17.9	42	32.8	4	5.4
Benzodiazepines	30	19	14	35.9	35	29.4	40	26.7	20	41.7	38	34.9	7	11.1	24	35.8	45	35.2	56	75.7

Major medical conditions	41	25.9	17	43.6	73	61.3	68	45.3	26	54.2	56	51.4	26	41.3	41	61.2	44	34.4	29	39.2

Table 2. Comparison between patients aged 50 years and older treated with antidepressants in general and psychiatric hospitals with respect to basic demographic and clinical characteristics

	Total sample (n=955)		General hospital sample (n=604)		Psychiatric hospital sample (n=351)		Statistics		
	N	%	N	%	N	%	$ç^2$	df	p
Male gender	375	39.3	222	36.8	153	43.6	4.3	1	**0.03**
Outpatient care	722	75.6	508	84.1	214	61.0	64.4	1	**<0.001**
Financial category							21.3	2	**<0.001**
High	465	48.7	326	54.0	139	39.6			
Upper middle	353	37.0	192	31.8	161	45.9			
Lower middle	137	14.3	86	14.2	51	14.5			
Principal psychiatric diagnosis							41.7	2	**<0.001**
Mood disorders	671	70.3	427	70.7	244	69.5			
Anxiety	130	13.6	102	16.9	28	8.0			
Schizophrenia	79	8.3	27	4.5	52	14.8			
Others	75	7.9	48	7.9	27	7.7			
Use of antidepressants									
TCAs	99	10.4	70	11.6	29	8.3	2.6	1	0.10
Tetracyclic	27	2.8	23	3.8	4	1.1	5.7	1	**0.01**
SSRIs	593	62.1	370	61.3	223	63.5	0.5	1	0.48
SNRIs	155	16.2	92	15.2	63	17.9	1.2	1	0.27
NaSSA	163	17.1	119	19.7	44	12.5	8.0	1	**0.005**
Others	127	13.3	78	12.9	49	14.0	0.2	1	0.64
SGAs	238	24.9	120	19.9	118	33.6	22.4	1	**<0.001**
FGAs	83	8.7	43	7.1	40	11.4	5.1	1	**0.02**
Mood stabilizers	204	21.4	125	20.7	79	22.5	0.4	1	0.51
Benzodiazepines	309	32.4	189	31.3	120	34.2	0.8	1	0.35
Major medical conditions	421	44.1	304	50.3	117	33.3	26.0	1	**<0.001**
	Mean	SD	Mean	SD	Mean	SD	T/Z	df	P
Age (years)	62.6	9.5	63.3	9.4	61.3	9.6	3.0	953	**0.003**
No. of depressive symptoms	3.4	2.0	3.5	2.0	3.3	2.0	-1.0	--[a]	0.3
No. of major medical conditions	0.5	0.8	0.7	0.9	0.3	0.5	-5.6	--[a]	**<0.001**

Bold values are p<0.05; a=Mann-Whitney U test; FGAs=first-generation antipsychotics; NaSSA=Noradrenergic and specific serotonergic antidepressant; SGAs=second-generation antipsychotics; SNRIs=Serotonin‑norepinephrine reuptake inhibitors; SSRIs=Selective serotonin reuptake inhibitors; TCAs=Tricyclic antidepressants

Table 3. Basic demographic and clinical data independently associated with older patients receiving antidepressant treatment in Asian psychiatric hospitals. Binary logistic regression analysis with treatment in general hospitals as reference

Variables	P value	OR	95% CI
Male gender	0.07	1.3	0.9-1.7
Outpatients	**<0.001**	0.2	0.1-0.3
Financial category			
High	**---**	1.0	---
Upper middle	**<0.001**	1.9	1.4-2.7
Lower middle	0.01	1.7	1.1-2.7
Principal psychiatric diagnosis			
Mood disorders	---	1.0	---
Anxiety disorders	**0.003**	0.4	0.3-0.7
Schizophrenia	**<0.001**	3.6	2.1-6.2
Others	0.60	1.1	0.6-2.0
Age (years)	0.83	0.9	0.9-1.01
No. of major medical conditions	**<0.001**	0.5	0.4-0.6
On Tetracyclic	**0.02**	0.2	0.1-0.8
On NaSSA	**0.008**	0.5	0.3-0.8
Use of SGAs	0.09	1.3	0.9-1.9
Use of FGAs	0.57	1.1	0.6-1.9

Bold values are $p<0.05$; study sites have been controlled for. FGAs=first-generation antipsychotics; NaSSA=noradrenergic and specific serotonergic antidepressant; SGAs=second-generation antipsychotics