# PREVALENCE AND RISK OF ANTIPSYCHOTIC POLYPHARMACY AMONG ELDER SCHIZOPHRENIA PATIENTS IN ASIA

**PENDYALA MEGANA[*1], PASUPULETI NEELIMA[1], Dr. V. Radhika reddy[2], Dr. Natta Pratibha[3] and Dr. K. Padmalatha[4]**

[*1]Pharm.D V Year, Department of Pharmacy Practice, Vijaya Institute of PharmaceuticalSciences for Women, Enikepadu, Vijayawada – 521 108, Andhra Pradesh, India.

[2]Professor and HOD, Department of Psychiatry, Old Government General Hospital, Benz Circle,Vijayawada – 520 004, Andhra Pradesh, India.

[3]Assisstant Professor, Department of Pharmacy Practice, Vijaya Institute of PharmaceuticalSciences for Women, Enikepadu, Vijayawada – 521 108, Andhra Pradesh, India.

[4]Professor & Principal, Department of Pharmacology, Vijaya Institute of PharmaceuticalSciences for Women, Enikepadu, Vijayawada – 521 108, Andhra Pradesh, India

**ABSTRACT:** Antipsychotic Polypharmacy (APP) is a controversial topic in the treatment of older adults with schizophrenia. APP is prescribing the multiple anti psychotics for individual patient to get symptoms relief by immediate therapeutic response and used in case of insufficient therapy or in treatment resistant conditions. Monotherapy is preferred as 1st line choice for management of symptoms but are in effective in 15 – 39 % of schizophrenia cases. APP causes extra pyramidal side effects and drug interactions in combinational regimen due to high dosage of drugs. Instead of these APP are highly effective then monotherapy. Prevalence rate of APP ranges from 4 - 92.2 % depending on patient population, diagnosis, study design and geographical region. The aim of this study was to know the use of antipsychotic polypharmacy (APP) pattern in Asian patients with schizophrenia and examine their prevalence and risk association.

**Study 1 -** is Cross sectional case record audit conducted at 32 centers in 6 - East Asian countries and territories (Taiwan, China, Japan, Hong Kong, Korea and Singapore) in July 2001.

**Study 2 -** was Research on Asian Psychotropic Prescription Patterns (REAP) project conducted in July 2001 followed by 2 waves of studies in July 2004 and October 2008 to March 2009.

**Study 3** - was REAP – AP4 project based on the dataset of the 4th survey conducted between March and May 2016.

Antipsychotic prescriptions of patients with schizophrenia from different countries and territories were evaluated. Daily doses of antipsychotic medications were converted to standard chlorpromazine equivalents (CPZ).

**KEYWORDS:** Antipsychotic Polypharmacy (APP), Schizophrenia, Monotherapy, Prevalence, Chlorpromazine equivalent (CPZ equivalent).

**INTRODUCTION:** Schizophrenia or Dementia praecox is severe psychiatric disorder in which people interpret reality abnormally that result in combination of delusions, hallucinations, loss of personality and extremely disordered behavior and thinking which has reduced life expectancy up to 20 % compared to healthy population. Antipsychotic medication (Neuroleptics) is 1st line treatment for schizophrenia to manage

core symptoms.[1]

First Generation Antipsychotics (FGAs) drugs are Haloperidol, Chlorpromazine, Flupentixol Decanoate, Fluphenazine Decanoate, Zuclopenthixol Decanoate, Loxapine, Mesoridazone, Molindone, Perphenazine, Pimozide, Prochlorperazine, Promazine, Chlorprothixene, Thiothixene, Trifluoperazine and Second Generation Antipsychotics ( SGAs) are Risperidone, Olanzapine, Clozapine, Quetiapine, Aripiprazole, Ziprasidone. Combinational usage of drugs is FGA + FGA, SGA + FGA, SGA + SGA. Anticholinergic drugs were used along with APP to treat frequent and severe Extrapyramidal Side Effects (EPS) induced by APP.[1, 2]

Antipsychotic Polypharmacy (APP) is associated with concurrent use of 2 or more chemically antipsychotic drugs to boost the therapeutic response in combinational usage of drugs in individual patient to manage schizophrenia spectrum disorders, which leads to higher daily dose prescribing and increased rate of adverse effects occurs due to long term utilization for treatment of disorder.[3]

The frequency of APP is 1st reported in 2008 study is 51.6 % in older Asian patients with schizophrenia. A meta-analytic review of 147 studies on APP shows global prevalence of 19.6

%, the extent of this practice varies, that ranges from 6 – 90 %, depending on geographical, clinical, regional, demographic and prescriber characteristics.[4] APP usually results in excessive antipsychotic doses that ranges from 10 – 30 % in schizophrenia depending on the treatment setting, patient population and methods used for operationalizing polypharmacy. Patients up to 15 – 39 % with schizophrenia do not respond to monotherapy that explains polypharmacy shows clinical benefits.[5]

Polytherapy gives advantage over monotherapy, in terms of efficacy without compromising on side effects burden as well as that impact on patient‟s quality of life, heavy financial burden, discontinuation rate, increased risk of hospitalization and mortality.

In comparison with younger patients, the older patients have poorer physical health, different psychopathology, increased use of multiple medications for co-morbid conditions, lower pharmacokinetics & pharmodynamics, age related hepatic & renal dysfunction and enhanced risk of drug - drug interactions such indicates the antipsychotic prescription patterns for elder patientswill differ from younger adults.

The aim of this study was to find out the use of antipsychotic polypharmacy (APP) in older Asian patients with schizophrenia and examine their demographic and clinical correlations. Information on hospitalized patients with schizophrenia aged 55 or older was extracted from the database of the Research on Asian Psychotropic Prescription Patterns study. Sociodemographic and clinical characteristics and antipsychotic prescriptions were analyzed.[6]

Only a few studies have examined the prescription pattern of APP in older patients withschizophrenia in Asia.[7]

Regular surveys of prescription patterns of psychotropic medications arean efficient way to examine the treatment rationale and trends over time.[8] The frequency of APPin older Asian patients with schizophrenia was first reported to be 51.6 % in a 2008 study.[9, 10, 11]

**METHODOLOGY:** This updated study examined the rate of APP in older adult patients withschizophrenia in Asia and its associated demographic and clinical factors. It was hypothesizedthat the rate of APP may be decreasing over time due to the increasing awareness of APP-relatedadverse effects in the study population groups.

**Study 1** - was a Cross sectional case record audit study conducted at 32 centers in 6 - East Asiancountries and territories (Taiwan, China, Japan, Hong Kong, Korea and Singapore) in July 2001. The study was approved by Research and Ethics Committees of all the coordinating centers. This study includes 2399 Inpatients of psychiatric units who fulfilled diagnostic criteria for schizophrenia in, ICD - 10 Revision or DSM-1V. Data was collected through a standardized datacollection form of defined population. Information collected from the case records includes age, gender, treatment setting, duration of illness and dose & type of psychotropic medications.

Data was analyzed by SPSS version 11.0 (SPSS Inc., Chicago, IL, USA) averages are reported as means ± standard deviation (SD), Normality of continuous distribution measures was checked with Kolmogorov–Smirnov one-sample test. One-way ANOVA for normally distributeddata and Mann–Whitney U-tests for non-normally distributed continuous data and by contingency for categorical variables, student‟s t-test for differences between the groups. Statistical significance was set at <0.05 (two-tailed).

**Study 2 -** was a Research on Asian Psychotropic Prescription Patterns (REAP) project it was conducted in July 2001 followed by 2 waves of studies in July 2004 and October 2008 to March 2009 using standardized protocol & same design in both studies. The participating countries and territories include Korea, China, Hong Kong, Japan, Singapore and Taiwan. Centers of India, Thailand and Malaysia joined the surveys in 2009. In this study, enrolled patients should follow the given criteria: ICD 10 or DSM IV for schizophrenia, 55 years and elderly aged, using antipsychotic drugs and ability to understand the study aims.

Review of medical records in 2001 includes age, sex, type and doses of antipsychotics, length ofillness, about significant psychotic symptoms in past month and extra pyramidal adverse effects (EPS). Along with review, patient interview was done in 2004 and 2009 using a questionnaire. Data was analyzed using Statistical Package for the Social Sciences version 13.0 for Windows. W2 tests were used for Comparisons between the 3 surveys with respect to APP prescribing patterns. Multiple logistic regression analysis with the „„Enter‟‟ method was used to understand the APP influencing demographic and clinical variables. The level of significance was two tailed& P = 0.05.

**Study 3 -** was REAP – AP4 project based on the dataset of the 4$^{th}$ survey conducted between March and May 2016. It comprises cross sectional surveys on the prescription pattern of psychotropic medications in schizophrenia and depression across Asia. The 1st REAP survey (REAP - AP1) was conducted in 2001, followed by REAP - AP2 in 2004 and REAP - AP3 in 2008 to 2009. Asian countries/territories participated in the REAP - AP4 survey.

**Study criteria:** Diagnosis of schizophrenia according to ICD 10 or DSM IV, treatment with psychotropic medications, inpatients or outpatients and aged 50 years or older. Patients using Type and dose of

antipsychotic medications and other psychotropic drugs, psychotic symptoms in the past month and extrapyramidal symptoms in the past 3 months were recorded.

Analysis of data is done through SPSS, version 2.0. Comparison between Antipsychotic Monotherapy (APM) and APP groups on bases of Demographic and clinical variables is done using independent sample t-test, w2 test for categorical variables and for continuous variables Mann-Whitney U test is used. Binary logistic regression analysis with the "Enter" method was used to determine the independent associations between demographic and clinical variables and APP. The level of significance was two tailed & p = 0.05.

**RESULTS:**

**Study 1:**

**Table 1 Demographic and Clinical Characteristics of study Population (N = 2399)**

| N | Japan (n = 627) | Singapore(n = 300) | Korea (n = 442) | China (n = 611) | Taiwan (n = 311) | HongKong (n = 108) | P - value |
|---|---|---|---|---|---|---|---|
| **Age (years)** | | | | | | | |
| **Mean** | 52.9 | 46.2 | 39.1 | 38.5 | 38.2 | 45.4 | <0.00 |
| **SD** | 13.5 | 10.8 | 9.5 | 12.9 | 10.8 | 13.5 | 1+/- |
| **Gender** | | | | | | | |
| **Male** | 58.4 | 58.7 | 57.0 | 50.9 | 55.6 | 58.3 | NS |
| **Female** | 41.6 | 41.3 | 43.0 | 49.1 | 44.4 | 41.7 | |
| **Duration of illness (%)** | | | | | | | |
| **< 1 year** | 2.7 | 1.3 | 3.9 | 11.5 | 1.0 | 00 | <0.00 1+/- |
| **1 - 5 years** | 6.7 | 7.3 | 12.0 | 20.4 | 12.8 | 7.4 | |
| **6 - 10 years** | 7.9 | 18.3 | 25.8 | 15.1 | 25.7 | 13.9 | |
| **11 - 20 years** | 16.9 | 41.0 | 40.7 | 24.8 | 34.9 | 25.9 | |
| **> 20 years** | 65.8 | 32.0 | 17.7 | 28.1 | 25.7 | 52.8 | |
| APP (%) | 78.6 | 70.3 | 35.5 | 25.2 | 22.2 | 12.0 | <0.00 1+/- |
| Atypical Antipsychotic & | 50.4 | 6.7 | 37.1 | 64.0 | 48.6 | 46.3 | <0.00 1+/- |
| Anticholinergic use (%) | | | | | | | |
| Treatment setting | 78.0 | 82.0 | 76.0 | 34.7 | 61.4 | 50.0 | <0.00 1+/- |
| Psychiatric hospital (%) | 78.1 | 100.0 | 38.7 | 67.3 | 100.0 | 100.0 | <0.00 1+/- |

**Figure 1 Number of Antipsychotics prescribed in different countries**

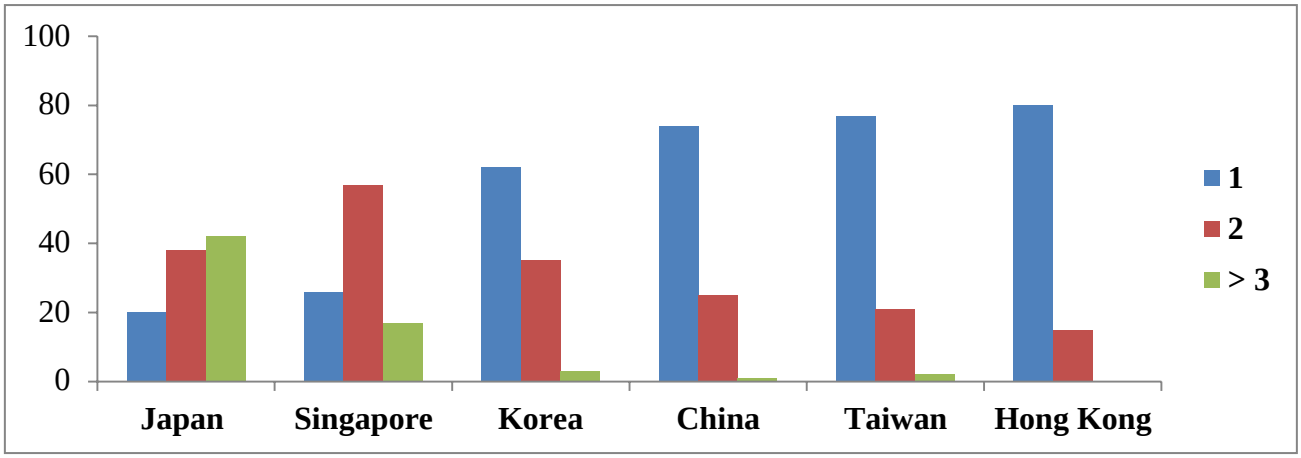



**Table 2 Comparison of characteristics between patients on one Antipsychotic (NP) andpatients on more than one Antipsychotic (P)**

| | NP (n = 1302) | P (n = 1097) | Test statistic | P - value |
|---|---|---|---|---|
| **AGE** | | | t = -7.81 d.f. = 2396 | < 0.001 |
| Mean | 41.66 | 45.93 | | |
| SD | 13.74 | 12.82 | | |
| Daily CPZ eq. (mg day$^{-1}$) | 411.47 | 983.10 | Z = -25.94 | < 0.001 |
| **DURATION OF ILLNESS** | | | | |
| < 1 year | 78 (6.00) | 33 (3.00) | | |
| 1 - 5 years | 199 (15.30) | 103 (9.40 ) | $X^2$ = 68.28 | < 0.001 |
| 6 - 10 years | 251 (19.30 ) | 152 (13.90) | | |
| 11 – 20 years | 369 (28.30) | 324 (29.50) | | |
| > 20 years | 405 (31.10) | 485 (44.20) | | |
| | | | OR (95 %S CI) | P |
| **GENDER** | | | | |
| Female | 606 (46.50) | 452 (41.20) | 1.00 | |
| Male | 696 (53.50) | 645 (58.80) | 1.24 (1.06, 1.46) | < 0.01 |
| **TREATMENT SETTING** | | | | |
| General hospital | 363 (72.10) | 245 (22.30) | 1.00 | |
| Psychiatric hospital | 939 (27.90) | 852 (77.70) | 1.34 (1.11, 1.62) | < 0.01 |
| **FIRST ADMISSION** | | | | |
| No | 1058 (81.26) | 898 (81.90) | - | NS |

| | | | | |
|---|---|---|---|---|
| Yes | 244 (18.74) | 199 (18.10) | - | |
| **MEDICATION USE** | | | | |
| Atypical antipsychotics | 620 (47.60) | 472 (43.00) | 0.83 (0.71,0.98) | < 0.05 |
| Anticholinergic drugs | 678 (52.10) | 850 (77.50) | 3.17 (2.65,3.79) | < 0.001 |

**Study 2:**

**Table 3 Socio-demographic and Clinical Characteristics of Older Asian Patients withSchizophrenia in REAP Surveys in 2001 – 2009**

| | **China (n = 215)** | | **Hong Kong (n = 43)** | | **Japan (n = 826)** | | **Korea (n = 128)** | | **ingapore(n = 84)** | | **Taiwan (n = 143)** | | **Total (n = 1439)** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** |
| Age (yrs) | 59.5 | 5.3 | 62.7 | 6.4 | 64.2 | 6.8 | 59.8 | 4.5 | 60.6 | 4.8 | 60.1 | 5.4 | 62.5 | 6.5 |
| CPZ Eq. mg/d | 431 | 334 | 404 | 379 | 636 | 616 | 577 | 528 | 429 | 410 | 394 | 311 | 557 | 540 |
| | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| Length of the illness < 5 yrs | 19 | 8.8 | 3 | 7.0 | 16 | 1.9 | 5 | 3.9 | 6 | 7.1 | 3 | 2.1 | 52 | 3.6 |
| Men | 114 | 53.0 | 23 | 53.5 | 436 | 52.8 | 54 | 42.2 | 45 | 53.6 | 81 | 56.6 | 753 | 52.3 |
| Positive Symptoms | 116 | 54.0 | 25 | 58.1 | 562 | 68.0 | 90 | 70.3 | 39 | 46.4 | 93 | 65.0 | 925 | 64.3 |
| Negative symptoms | 151 | 70.2 | 28 | 65.1 | 597 | 72.3 | 64 | 50.0 | 34 | 40.5 | 86 | 60.1 | 960 | 66.7 |
| EPS | 32 | 14.9 | 24 | 55.8 | 270 | 32.7 | 38 | 29.7 | 8 | 9.5 | 56 | 39.2 | 428 | 29.7 |
| TD | 13 | 6.0 | 11 | 25.6 | 74 | 9.0 | 6 | 4.7 | 3 | 3.6 | 23 | 16.1 | 130 | 9.0 |
| FGA | 82 | 38.1 | 19 | 44. | 588 | 71.2 | 89 | 69.5 | 72 | 85.7 | 56 | 39.2 | 906 | 63.0 |
| SGA | 161 | 74.9 | 22 | 51.2 | 513 | 62.1 | 61 | 47.7 | 7 | 8.3 | 97 | 67.8 | 861 | 59.8 |
| APP | 58 | 27.0 | 18 | 41.9 | 544 | 65.9 | 46 | 35.9 | 51 | 60.7 | 25 | 17.5 | 742 | 51.6 |

**Table 4 Demographic and Clinical Correlates Associated with APP in Sample (n = 1439)**

| | P | Odds ratio | 95 % CI |
|---|---|---|---|
| **Age in yrs.** | 0.2 | 1.0 | 0.96 - 1.01 |
| **Antipsychotic dose, CPZ eq. mg/d** | < 0.001 | 1.003 | 1.002 – 1.003 |
| **Length of illness** | 0.8 | 0.9 | 0.4 – 1.9 |
| **Male Gender** | 0.2 | 1.2 | 0.9 - 1.6 |
| **Positive symptoms** | 0.8 | 1.0 | 0.8 – 1.4 |
| **Negative symptoms** | 0.99 | 1.0 | 0.7 – 1.4 |
| **EPS** | 0.9 | 1.0 | 0.7 - 1.4 |
| **TD** | 0.2 | 0.7 | 0.4 - 1.2 |
| **FGAs** | < 0.001 | 10.9 | 7.8 - 15.4 |
| **STUDY SITES** | | | |
| **China** | - | 1.0 | - |
| **Hong Kong** | 0.005 | 3.2 | 1.4 – 7.1 |
| **Japan** | < 0.001 | 3.9 | 2.5 – 5.9 |
| **Korea** | 0.03 | 0.5 | 0.3 – 0.95 |
| **Singapore** | 0.002 | 2.8 | 1.5 - 5.5 |
| **Taiwan** | 0.005 | 0.4 | 0.2 – 0.8 |
| **STUDY TIME** | | | |
| **2001 survey** | - | 1.0 | - |
| **2004 survey** | 0.2 | 1.3 | 0.9 - 1.8 |
| **2009 survey** | < 0.001 | 2.0 | 1.4 – 3.0 |

**Table 5 Comparison of Prescribing Patterns of APP in Older Asian Patients withSchizophrenia in 2001, 2004, 2009**

| | 2001 | | 2004 | | 2009 | | Statistics | | |
|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | $X^2$ | df | P |
| **FGA + FGA** | 177 | 36.1 | 73 | 16.4 | 44 | 8.7 | 121.0 | 2 | <0.001 |
| **SGA+ SGA** | 12 | 2.4 | 22 | 4.9 | 62 | 12.3 | 42.0 | 2 | <0.001 |
| **FGA + SGA** | 97 | 19.8 | 123 | 27.6 | 132 | 26.2 | 9.0 | 2 | 0.01 |

**STUDY 3:**

**Table 6 Basic demographic and clinical characteristics of the study samples**

| | Total sample (N = 879) | | APM (n = 523) | | APP (n = 356) | | Statistics | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | t/x | df | P |
| Age (years) | 58.0 | 6.7 | 58.1 | 6.8 | 57.8 | 6.5 | 0.56 | 877 | .57 |
| AP dose CPZ eq. mg/d | 408 | 385 | 283 | 268 | 590 | 452 | -13.02 | - | < 0.01 |
| BMI | 23.9 | 4.4 | 24.1 | 4.3 | 23.6 | 4.4 | 1.61 | 877 | .10 |
| | N | % | N | % | N | % | $X^2$ | df | P |
| Male | 415 | 47.2 | 244 | 46.7 | 171 | 48.0 | 0.16 | 1 | .68 |
| Age(years) | | | | | | | 0.42 | 1 | .51 |
| 50 - 64 | 732 | 83.3 | 432 | 82.6 | 300 | 84.3 | | | |
| 65 & older | 147 | 16.7 | 91 | 17.4 | 56 | 15.7 | | | |
| In-patient | 513 | 58.4 | 271 | 51.8 | 242 | 68.0 | 22.76 | 1 | <0.001 |
| Illness duration | | | | | | | 7.98 | 1 | 0.005 |
| < 5 years | 113 | 12.9 | 81 | 15.5 | 32 | 9.0 | | | |
| > 5 years | 766 | 87.1 | 324 | 91.0 | 442 | 84.5 | | | |
| Positive symptoms | 500 | 56.9 | 277 | 53.0 | 223 | 62.6 | 8.08 | 1 | 0.004 |
| Negative symptoms | 425 | 48.4 | 239 | 45.7 | 186 | 52.2 | 3.63 | 1 | 0.056 |
| Acute EPS | 294 | 33.4 | 165 | 31.5 | 129 | 36.2 | 2.09 | 1 | 0.14 |
| TD | 31 | 3.5 | 21 | 4.0 | 10 | 2.8 | 0.90 | 1 | 0.34 |
| Antidepressants | 115 | 13.1 | 73 | 14.0 | 42 | 11.8 | 0.86 | 1 | 0.35 |
| Mood stabilizers | 117 | 13.3 | 58 | 11.1 | 59 | 16.6 | 5.51 | 1 | 0.19 |
| Benzodiazepines | 274 | 31.2 | 167 | 31.9 | 107 | 30.1 | 0.34 | 1 | 0.55 |
| Anticholinergics | 393 | 44.7 | 208 | 39.8 | 185 | 52.0 | 12.74 | 1 | <0.001 |
| FGA | 251 | 28.6 | 88 | 16.8 | 163 | 45.8 | 87.08 | 1 | <0.001 |
| SGA | 700 | 79.6 | 394 | 75.3 | 306 | 86.0 | 14.73 | 1 | <0.001 |
| Country/ territory | | | | | | | 59.89 | 14 | <0.001 |

**Figure 2 APP in older adult patients with schizophrenia in 15 Asian countries/territories**

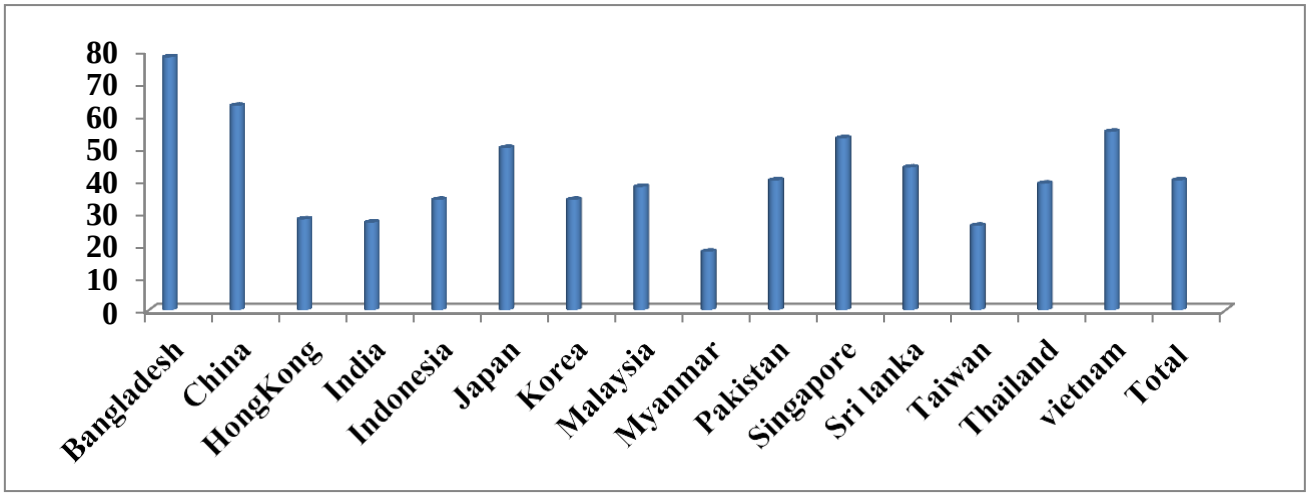
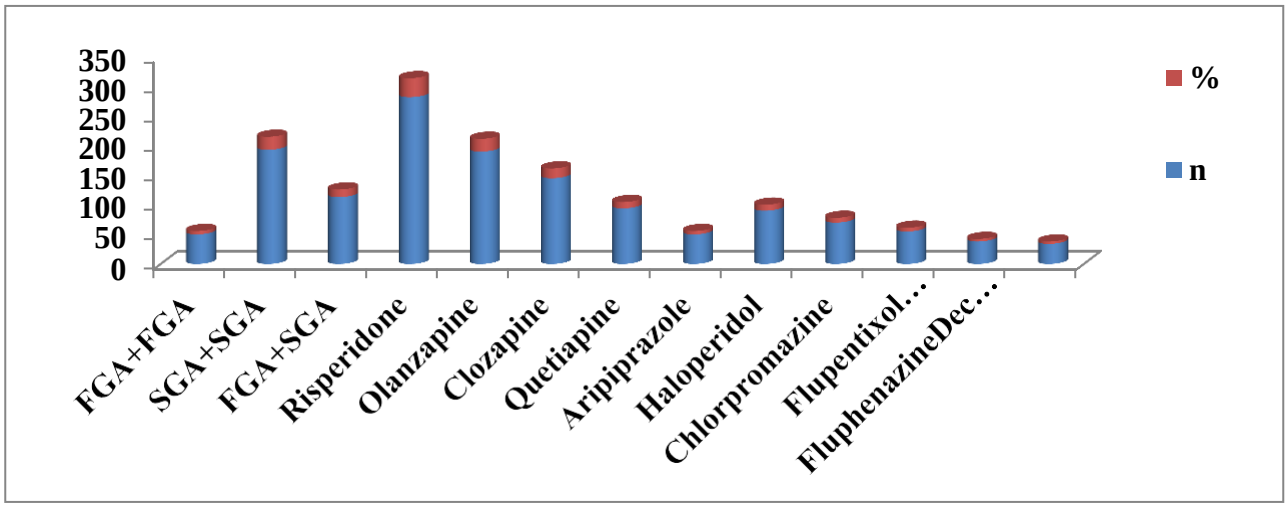



**Table 7 Independent Demographic & clinical correlates of APP**

| Variables | P value | Odds ratio | 95 % CI |
|---|---|---|---|
| **AP dose, CPZ eq. mg/d** | < 0.001 | 1.003 | 1.002 - 1.003 |
| **Outpatient** | 0.77 | 0.945 | 0.636 - 1.405 |
| **Duration of illness (> 5 yrs)** | 0.02 | 1.845 | 1.087 - 3.132 |
| **Positive symptoms** | 0.052 | 1.419 | 0.998 - 2.019 |
| **Negative symptoms** | 0.19 | 0.794 | 0.560 - 1.125 |
| **Mood stabilizers** | 0.71 | 0.916 | 0.572 - 1.468 |
| **Anticholinergics** | < 0.01 | 1.871 | 1.329 - 2.635 |
| **SGA** | 0.001 | 2.264 | 1.453 - 3.529 |

**Figure 3 The prescription patterns & most commonly prescribed Antipsychotics drugs inolder adult patients with schizophrenia in Asia**



**Discussion:**

**Study 1:** In table 1 showing Case records of 2399 patients, APP seen in 45.7 % of patients (n =1097) was commonly seen in Japan, followed by Singapore, Korea, China, Taiwan, Hong Kong. Figure 1 showing number of drugs, more than 3 - Antipsychotics were prescribed in Japanfollowed by Singapore and up to 2 - antipsychotics was prescribed highly in Singapore, Japan,Korea, china, Hong Kong. Antipsychotic polypharmacy regimen was mainly seen in elderly age,male gender, treatment in psychiatric hospital setting, enhanced use of Anti cholinergics, countrywise distribution, younger age and longer duration of illness was shown in table 2.

**Study 2:** Out of 1439 patients, 742 patients received (51.6 %) of the patients were prescribedwith APP in the 3 - REAP surveys; 286 (58.4 %) in 2001, 218 (48.9 %) in 2004 and 238 (47.3

%) in 2009, the number is higher than the 10 – 30 % for Western patients diagnosed with schizophrenia. The demographic studies of table 2 shows difference in APP prescription in various study sites varying from 17.5 % in Taiwan, 60.7 % in Singapore, 27 % in china, 41.9 % in Hong Kong, 35.9 % in Korea, 65.9 % in Japan. It represents that factors are independently associated with APP; patients who are on APP are prescribed with higher dose of antipsychotics and most likely First generation antipsychotics.

According to table 3, 1439 patients satisfy the study criteria were included in study in which 490 patients in 2001, 446 patients in 2004 and 503 in 2009. Out of 1439 patients, 742 patients

received APP (51.7 %) in the 3 - REAP surveys: 286 (58.4 %) in 2001, 218 (48.9 %) in 2004 and 238 (47.3 %) in 2009. Because SGAs were efficacy over FGA, less risk of EPS and the cost effectiveness of SGAs. The of use atypical antipsychotics was increased.

**Study 3:** As per table 1, total of 879 older schizophrenia patients were included in survey. Mean age of the sample is 58.0 + 6.7 years. Male are 47.2 %. In that SGAs are prescribed in high rateat both APP and APM. Compared to APP anti cholinergics are prescribed more in APM.According to Figure 2, the percentage of APP utilization in this countries was 356 (40.5 %) with

77.8 % in Bangladesh, 63.6 % in China, 54.7 % in Vietnam, 52.3 % in Singapore, 50.5 % in japan, 48.4 % in Thailand, 44.0 % in Sri Lanka, 40.0 % in Pakistan, 37.7 % in Malaysia, 34.4 % in Indonesia, 34.5 % in Korea, 28.6 % in Hong Kong, 28.0 % in India, 26.1 % in Taiwan and

18.5 % in Myanmar.

The results of country/territory-adjusted regression model were given after excluding FGA in table 2. Higher antipsychotic doses, longer duration of illness, use of anticholinergics and SGA are associated with APP. Logistic regression analysis was conducted after excluding SGA from variables. Higher AP doses, long term duration of illness and use of FGA & anticholinergics were associated with APP.

Based on Figure 2, the prescription patterns & Most commonly prescribed Antipsychotics drugs in Older adult patients with schizophrenia in Asia are Resperidone, Followed by Olanzapine & 2

- SGA drugs, Clozapine, FGA + SGA, Quetiapine, Haloperidol, Chlorpromazine, Flupentixol deconate, Flupenazine deconate, Zuclopentixol deconate, FGA +FGA drugs.

**Limitations:**

**Study 1:** first it was the clinical audit report, so that standardized ratings of clinical characteristics such as psychopathology and adverse effects were not conducted. Second, being a cross-sectional study it did not allow for any firm conclusions about the relationship between APP and its correlates. Third the results may not be applicable be generalizable to community based patients or outpatients.

**Study 3: 1.** The **s**tudy was done in a systemic rather than a random manner. **2.** Important APP variables, such as age of onset, severity of symptoms, health insurance and socioeconomic status were not available in the databases. **3.** In cross-sectional design of the REAP-AP surveys, safety and effectiveness of APP could not be determined. **4.** Most of the samples obtained from inpatient settings. So, these findings are not applicable to community-dwelling patients. Furthermore, the prescribing pattern observed in this small sample could not be applied to all prescription procedures in Asia. **5.** The rationale for the use of APP could not be discussed asthis information was not collected in this survey.

**Conclusion:** Polypharmacy with male gender shows the biases and perception of male inpatients will present with severity of illness, aggression and agitation or able to tolerate combinational therapy. Increased age of the patients and greater length of illness shows longer period of exposure to antipsychotics that increases the risk of extrapyramidal side effects. The association of polypharmacy with less use of atypical antipsychotic further increases and compounds theside effect burden for management use of anticholinergic drugs was increased.

Prescription with too many drugs is depending on clinical, social, cultural factors. Rates of antipsychotic polypharmacy in Hong Kong & Taiwan were low compared to other countries. Polypharmacy used for better symptom relief and with less occurrences of side effects in case of higher doses of any single antipsychotic drugs.

Younger patients presenting with severe psychotic symptoms in early stage of schizophrenia, resulting in frequent use of APP. Reasons for APP prescription are inpatients admit with severe symptoms and mostly those are treatment resistant, that increases APP use. And common belief in Asian countries that combination of medicines with different pharmacological components is highly effective. In older patients due to higher risk of medication induced side effects clinicians were prescribed drugs with caution. Reasons for High APP is economic and socio-cultural factors in prescribing practice, professional and public attitude toward APP, local prescribing guidelines, health insurance policies.

Polypharmacy is associated with excessive dosing of antipsychotics leads to increased risk of side effects such as extra pyramidal symptoms (EPS) and metabolic syndrome. To prevent the occurrences of EPS induced by APP use of anticholinergics was increased. Long term use of Anticholinergics may increase the risk of cognitive dysfunction and mortality in older patients.In this study commonly prescribed SGAs in older patients are Olanzapine and Resperidone.

**Conflict of interest:** The authors who have taken part in this study declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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