

# A Review of Schizophrenia Research in Malaysia

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## SUMMARY

Research in schizophrenia has advanced tremendously. One hundred and seventy five articles related to Schizophrenia were found from a search through a database dedicated to indexing all original data relevant to medicine published in Malaysia between the years 2000-2013. This project aims to examine published research articles, in local and international journals in order to provide a glimpse of the research interest in Malaysia with regards to schizophrenia. Single case study, case series report, reviews and registry reports were not included in this review. Medication trial, unless it concerned a wider scope of psychopharmacology was also excluded from this review. A total of 105 articles were included in this review. Despite numerous genetics studies conducted and published, a definitive conclusion on the aetiology or mechanism underlying schizophrenia remains elusive. The National Mental Health - Schizophrenia Registry (NMHR) proved to be an important platform for many studies and publications. Studies stemmed from NMHR have provided significant insight into the baseline characteristic of patients with schizophrenia, pathway to care, and outcomes of the illness. International and regional collaborations have also encouraged important work involving stigma and discrimination in schizophrenia. Ministry of Health's hospitals (MOH) are the main research sites in the country with regards to schizophrenia research. Numbers of schizophrenia research are still low in relation to the number of universities and hospitals in the country. Some of the weaknesses include duplication of studies, over-emphasising clinical trials and ignoring basic clinical research, and the lack of publications in international and regional journals.

**KEY WORDS:** schizophrenia, registry, Malaysia

## INTRODUCTION

Research in schizophrenia has advanced tremendously. This project aims to examine the published research articles, in local and international journals in order to provide a glimpse of the research interest involving schizophrenia in Malaysia. Single case study, case series report, reviews and registry reports were not included in this review. Medication trial, unless it concerned a wider scope of psychopharmacology was also excluded from this review. Therefore only 105 of the 175 articles found on schizophrenia were included in this review.

## SECTION 1: REVIEW OF LITERATURE

The formation of the National Mental Health Registry (NMHR) for schizophrenia was one the important milestone of local schizophrenia research. On 1 January 2003, the NMHR was

formed by the Ministry of Health (MOH) Malaysia to collect information about people with mental disorders in Malaysia. Schizophrenia was the first mental disorder targeted by the NMHR. The registry collects information about patients with schizophrenia in Malaysia to evaluate the risk factors and treatment in the country, which will facilitate the planning and evaluation of mental health services in the country. In 2003, all 29 departments of psychiatry from the MOH and four local university hospitals participated in data collection. This was a coverage rate of 90.6%. By 2005, 74 primary health-care centres and hospitals throughout the country participated in data collection. The Mental Health Registry Unit (MHRU) was established to monitor the process of data collection throughout the country, which includes data entry, analysis and reporting. The NMHR for schizophrenia published its first paper in 2008 in the Medical Journal of Malaysia. The paper provided detailed information about the profile of person with schizophrenia presented for the first time to various psychiatry and mental health providers throughout Malaysia. The incidence rate reported in the paper was 7.7-43.0 per 100,000 population. Unemployment rate was as high as 70%. Duration of untreated illness was at a median of 12 months and 20% of them suffered from at least one form of comorbidity<sup>1</sup>.

In 2012, NMHR for schizophrenia published its first paper on the one-year outcome of patients who were registered in 2004 and 2005. Of the 2604 registered patients with FES, only 37.7% had their outcomes successfully assessed. Among those assessed, 25.5% were lost to follow-up and 45.8% were followed-up in different centres. Only two patients committed suicide. Comparison of types of antipsychotic medications use between baseline and at one-year follow-up is shown in Fig. 1. Increases in weight gain and body mass index were major concerns. On a positive note, employability improved. Forty percent of the patients had their antipsychotics changed over the one-year period but about 20% of patients were on polytherapy at baseline and after one year. The use of anticholinergic medication dropped remarkably after the one-year treatment period<sup>2</sup>.

In 2005, Esther et al from University Malaya Medical Centre (UMMC) reported an outcome study of early onset schizophrenia, defined as the onset of illness before 18 years old. About half of the subjects had an unfavourable outcome, with significantly younger (<15 years old) age of onset of illness, longer duration of symptoms prior to their first contact, and impaired functioning<sup>3</sup>.

## GENETICS RESEARCH

Genetics research in schizophrenia is relatively new in Malaysia and all the publications in this area occurred within the last five years. The Department of Chemical Engineering of Tunku Abdul Rahman University (UTAR) had published a

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substantial number of papers in genetic research in schizophrenia. Tee *et al.* from UTAR found a possible association between genotype distribution dopamine receptor (DRD3) polymorphism and schizophrenia in a Malay sample population<sup>4</sup>; they also found that tryptophan hydroxylase 2 gene (TPH2) was not associated with schizophrenia in the same ethnic population<sup>5</sup>, and there was no significant association between DRD3 Ser9Gly polymorphisms and catechol-O-methyltransferase (COMT) and schizophrenia in Malays<sup>6</sup>. The same research group, however, found highly significant association between the COMT gene and schizophrenia<sup>7</sup>. Another research group from UTAR led by Loh *et al.* failed to demonstrate the association between neuregulin-1 with schizophrenia in Malays, Chinese and Indians in Malaysia<sup>8</sup>. The same group also found no association between AKT1 gene variants and schizophrenia<sup>9</sup>, and brain-derived neurotrophic factor (BDNF) and dopamine- and cAMP-regulated phosphoprotein (DARPP-32) genes were not risk factors for schizophrenia in the Malay population<sup>10</sup>.

Zahari *et al.* from the Institute for Research in Molecular Medicine, Universiti Sains Malaysia (USM) looked into the influence of the dopamine D2 receptor (DRD2) polymorphisms on the clinical outcomes of people with schizophrenia. DRD2 polymorphism might have implications for the symptoms of schizophrenia and a predictor of treatment outcomes. Patients with Cys311 allele were found to have more severe symptoms of schizophrenia and worse treatment response<sup>11</sup>. Zalina *et al.* from USM studied the relationship between CYP2D6 polymorphisms on symptomatology in patients with schizophrenia; and it was found that CYP2D6 polymorphisms were significantly associated with negative symptoms of schizophrenia but not with the motor side effect of antipsychotics<sup>12</sup>. Zain *et al.* from the Department of Pharmacy, University Malaya (UM) found significant association between rs7690296 single nucleotide polymorphism and schizophrenia for Malays and Indians<sup>13</sup>. Wan *et al.* from the same department in UM demonstrated that COMT functional polymorphism of Val158Met had a weak association with schizophrenia and did not play a major role in susceptibility to schizophrenia<sup>14</sup>.

#### ACCESS TO CARE

The pathway to care in schizophrenia is important because it gives us an understanding on how a patient eventually obtains mental health care from the moment symptoms occur. With this knowledge, providing optimal care to reduce the duration of untreated psychosis (DUP) or illness is possible. Almost all the information in this area came from the NMHR for schizophrenia and schizophrenia patients from Kuala Lumpur Hospital (HKL). Phang *et al.* found that even though consultation from traditional healers was common and popular prior to mental health consultation, it was not associated with treatment delay and traditional healers in an urban setting may even be a potential collaborator to manage patients with schizophrenia<sup>15</sup>. Half (54%) of the patients had at least one contact with traditional healer but only 7.4% of them reported beneficial effects from it<sup>16</sup>. He also found the commonest reason for treatment delay was lack of knowledge by patients and family members that the mental state changes were due to mental illness<sup>17</sup>. A study in Kota Kinabalu by Swami *et al.* from the University of Westminster, London, UK, Sabah reported that the public believed schizophrenia was sinful and mental hospitals could not provide effective treatments<sup>18</sup>.

In a larger scale, Chee *et al.* who examined DUP using data from NMHR found the mean DUP in Malaysia was 37.6 months and the indigenous community had the shortest DUP compared to Malays, Chinese and Indians. Being a female,

having less education, and having comorbidities were related to longer DUP<sup>19</sup>.

#### CLINICAL FEATURES

The symptoms profile of schizophrenia has been extensively researched in Malaysia for the last 10 years. McLean *et al.* from the Queensland Centre for Mental Health Research in Australia published two articles on schizophrenia symptoms among the Iban community of Sarawak. They found distinct symptom profile in this community, in which they exhibited less thought disorders but more hallucinations and disorganised behaviours. Ibans also demonstrated shorter prodrome, higher use of substance, and older age for the onset of psychosis compared with Australian and Indian populations<sup>20,21</sup>. Gill *et al.* from the UMMC in Malaysia studied the characteristics of first episode psychosis among the Malaysian Chinese and found the most common symptoms were functional decline, sleep disturbance and dysphoric mood. The drawback of this study was that there was no comparison with other ethnic groups<sup>22</sup>. Nor Zuraida *et al.* from the same centre reported no gender differences in terms of psychopathology and functionality among patients with schizophrenia<sup>23</sup>.

Lack of insight has been a common feature in schizophrenia and it has been one of the most significant factors contributing to medication non-adherence. Ting *et al.* from UMMC studied schizophrenia patients in Permai Hospital, one of the largest mental institutions in Malaysia, and found 54% of them had moderate to poor insight<sup>24</sup>. Sharmilla and Hatim from the same centre who later compared insight among patients with schizophrenia and other mood disorders with psychosis found that schizophrenia patients had the worst insight. The level of impairment of insight was associated with functionality of patients<sup>25</sup>.

Rusdi *et al.* from UMMC studied schizophrenia patients with regards to substance use in Hospital Bahagia Ulu Kinta (HBUK), the largest mental institution in Malaysia. Based on the admission registry in HBUK, 24% of schizophrenia patients had a history of substance use. Those on cannabis had the highest prevalence for schizophrenia and male patients with a history of substance use were also more likely to exhibit aggression<sup>26</sup>. Abdul Hamid and Abdul Razak from the National University Hospital and Kuala Lumpur Hospital reported that 15% of schizophrenia outpatients had second diagnosis of obsessive-compulsive disorder (OCD). They did not find any differences in demographic and neurocognitive function for schizophrenia with and without OCD<sup>27</sup>. Ong *et al.* from the USM in 2013 reported high prevalence of sexual dysfunction (ranging from 78.4% to 97.1%) among schizophrenia outpatients in Taiping Hospital; with orgasmic dysfunction being least impaired and satisfaction during intercourse as the worst impaired<sup>28</sup>.

Cognitive impairment in schizophrenia, specifically verbal memory performance among schizophrenia patients were studied by Zahiruddin *et al.* and Hazura *et al.* from USM. Using the Malay version of the Auditory Verbal Learning Test, they were able to demonstrate that schizophrenia patients had significantly worse verbal memory and this was significantly correlated with occupational status, educational level, and negative symptoms of schizophrenia. Depressive symptoms and smoking were not found to be correlated with verbal memory performance<sup>29,30</sup>. Zakaria *et al.* from National University of Malaysia (UKM) examined motor neurological soft signs among schizophrenia patients, and found 68.8% of them had motor neurological soft signs and this was associated with a wide range of clinico-demographic and neurocognitive factors<sup>31</sup>.

Among the forensic patients with schizophrenia, Surina *et al* from USM studied the forensic patients in Hospital Bahagia in terms of the relationship between psychopathology and the offenders' characteristic. They showed that the offenders with schizophrenia received treatment at a later age. Those who were considered to be of unsound mind at the time of offence had significantly more positive symptoms<sup>32</sup>.

Roseliza-Murni *et al* from the UKM studied the relationship between expressed emotion (EE) among the caregivers and relapse rate of patients. They found that high EE was associated with eight times the risk of illness relapse. Critical comments and the caregivers' extraversion personality trait were the strongest predictors<sup>33</sup>.

### OBESITY & METABOLIC SYNDROME

Obesity and metabolic syndrome are among the major medical comorbidities in schizophrenia. Several hospital-based studies were carried out to address the issue of obesity in schizophrenia. Salmi *et al* from the UKM did a cross-sectional study on schizophrenia patients and found 35.1% of them were categorised as obese and 39.2% as overweight. There were more Malays and Indians who were overweight. The risk factors were being male and having a lower total income<sup>34</sup>. Norlelawati *et al* carried out a similar study in Tengku Ampuan Afzan Hospital, Kuantan and found schizophrenia patients were twice as likely as the general population to develop obesity and this was seen across all the main ethnic groups in Malaysia<sup>35</sup>. Ainsah *et al* from UKM studied the possible relationship between binge eating, lifestyle and obesity in schizophrenia but could not establish any such associations<sup>36</sup>. Fairuz *et al* from the same centre examined the prevalence of insulin resistance among schizophrenia patients in UKM and found 68% of them had insulin resistance. Univariate analysis found body-mass index (BMI) and waist circumference to be associated with insulin resistance although this significance disappeared in multivariate analysis<sup>37</sup>.

The relationship between weight gain or metabolic syndrome and antipsychotic medications were widely studied in Malaysia. Using the National Mental Health Registry for schizophrenia, Chee *et al* reported on weight changes among first-episode schizophrenia one year after the initiation of antipsychotic medications. At the time of diagnosis, mean weight for patients being treated with first-generation antipsychotics (FGAs) was 57.5±12.3 kg, and mean weight for patients with second-generation antipsychotics (SGAs) was 61.0±22.0 kg. The mean weights did not differ significantly at the time of diagnosis ( $P = 0.110$ ). Patients treated with FGAs and SGAs gained significant amount of weight after one year ( $P < 0.001$  for both groups). Mean weight gain for FGAs (6.6±8.5 kg; median, 5 kg) was slightly less than that for SGAs (9.7±9.3 kg; median, 7 kg). Body mass index for FGAs at diagnosis was 21.4±4.0 kg/m<sup>2</sup> (median, 20.8 kg/m<sup>2</sup>), and that for SGAs was 23.0±7.0 kg/m<sup>2</sup> (median, 21.6 kg/m<sup>2</sup>). Body mass index had increased significantly in both groups after one year of treatment but did not differ significantly at baseline ( $P = 0.594$ ) and after treatment ( $P = 0.105$ ) between the two groups. Patients treated with olanzapine had the biggest mean weight gain with treatment (ie, 14.3±10.1 kg)<sup>38</sup>.

Mas Ayu *et al* from UMMC studied the prevalence of metabolic syndrome among schizophrenia patients on monotherapy antipsychotics. The prevalence of metabolic syndrome was 46.7% and more were taking SGAs. They found patients treated with the antipsychotics trifluoroperazine, flupenthixol decanoate, and clozapine to be associated with the highest prevalence of metabolic syndrome<sup>39,40</sup>. Ruzanna *et al* from UKM

who studied the association between dyslipidaemia and types of antipsychotics failed to identify a significant difference between FGAs and SGAs although 66% of patients with chronic schizophrenia developed dyslipidaemia<sup>41</sup>. Ainsah *et al* from the same centre who studied the relationship between obesity and types of antipsychotic use also failed to find a significant difference between FGAs and SGAs. In this study, 71.4% of SGAs and 79.4% of FGAs were at least overweight<sup>42</sup>.

Various genetic polymorphisms have been implicated in antipsychotic-induced weight gain. Roffeei *et al* from UMMC found patients that carried the ADRA2A rs1800544 GG genotype and the MTHFR rs1801131 C were associated with BMI reduction when their treatment was switched to aripiprazole and ziprasidone<sup>43</sup>.

### MANAGEMENT

#### Psychopharmacology

A study on the prescription pattern of medication use in schizophrenia was carried out at the Tengku Ampuan Rahimah Hospital psychiatric outpatient unit. The commonest antipsychotic was haloperidol (16.3%), average daily dose was 342.06 mg chlorpromazine equivalent. Thirty-two percent of the entire patients sample was prescribed with second-generation antipsychotics. The commonest SGA was olanzapine, followed by risperidone and quetiapine. Only 3.2% of those patients given SGA received clozapine<sup>44</sup>.

Since 2009, Kuala Lumpur Hospital, Malaysia has been part of the Research on Asia Psychotropic Prescription (REAP) study group. This group is an ongoing pharmaco-epidemiological investigation of psychotropic drug prescription trends in schizophrenia inpatients in Asia. The participating countries and regions include Mainland China, Hong Kong, Japan, Korea, Singapore and Taiwan. Each centre used the same standardised protocol and data collection procedure. Centres in India, Malaysia and Thailand joined the project in 2009. The three REAP surveys to date were conducted in July 2001, July 2004 and from October 2008 to March 2009. Below is a summary of the study's findings;

1. Univariate analyses in the use of antipsychotics found the following factors to be significantly associated with the male sex: a younger age, higher doses of antipsychotics, less prominent delusions and hallucinations, more prominent negative symptoms, less likelihood of a prescription for SGAs, greater use of antipsychotic polypharmacy, mood stabilisers (MS) and depot antipsychotics, more frequent tardive dyskinesia (TD), and less weight gain<sup>45</sup>.
2. The frequency of tardive dyskinesia (TD) was 5.0% with wide variations between countries (0 – 14.9%). Malaysia's rate was 1.2%. Multiple logistic regression analysis showed that the following variables were independently associated with TD: study time, study site, older age, male gender, more severe negative and extrapyramidal symptoms and less anti-cholinergic drugs<sup>46</sup>.
3. Adjunctive benzodiazepine treatment of in-patients diagnosed with DSM-IV or ICD-10 schizophrenia has been prevalent in Asia over the past decade, averaging 54% of over 6700 schizophrenia patients sampled at 12 centres in nine countries. Use of adjunctive benzodiazepines was associated with prominent positive psychotic symptoms (delusions and hallucinations), aggressive behaviour, and occupational or social dysfunction. Moreover,



- benzodiazepines also were associated with use of other drugs, notably MS and antidepressants, in addition to common use of anti-parkinsonian agents. Prevalence of benzodiazepine (BZD) in Malaysia was 59%, daily diazepam-equivalent of  $18.7 \pm 14.1$  mg<sup>47</sup>.
4. The frequency of reported sexual dysfunction (SD) in the whole sample, in women, and in men were 3.0%, 0.8%, and 4.6%, respectively, with variations across study sites. Twelve percent of patients in Malaysia reported SD. In the multivariate analyses, male sex, more SGA, BZD, and antidepressants were independently associated with higher likelihood of reported SD, whereas negative symptoms had an inverse association with reported SD<sup>48</sup>.
  5. MS were given to 20.4% (n=1377/6761) of hospitalised schizophrenia patients, with increased usage over time. MS use was significantly and independently associated in multivariate logistic modelling with aggressive behaviour, disorganised speech, year sampled (2008 vs. earlier), multiple hospitalisations, less negative symptoms, and younger age. There were regional variations (Japan, Hong Kong, Singapore, Taiwan or China)<sup>49</sup>.
  6. The proportion of antipsychotic polypharmacy (APP) prescription decreased from 46.8% in 2001, to 38.3% in 2004, and increased to 43.4% in 2009, with wide inter-country variations at each survey. Forty-nine percent of schizophrenia patients in Malaysia received APP prescription. Multiple logistic regression analysis of the whole sample revealed that patients on APP were younger, had a higher dose of antipsychotics in chlorpromazine equivalents, and more severe positive and negative symptoms. They were also more likely to receive depot and first-generation antipsychotic drugs<sup>50</sup>.
  7. The frequency of anticholinergic medication (ACM) prescription in older patients (65 years and older) was 64.6% in the pooled sample, with 72.4%, 61.9%, and 59.5% in 2001, 2004, and 2009, respectively. In Malaysia, 25% of the older patients were given ACM. Multiple logistic regression analysis of the whole sample revealed that patients on ACM had a higher dose of antipsychotic medications, and were more likely to have extrapyramidal side effects and receive first-generation antipsychotic medications<sup>51</sup>.
  8. The frequency of MS prescription in older Asian was 26.7% in the pooled sample, with 25.5% in 2001, 26.9% in 2004 and 27.7% in 2009. No prescriptions were found in the Malaysian sample. The corresponding figures for BZD were 20.7% (pooled sample), 20.2% (in 2001), 18.4% (in 2004) and 23.1% (in 2009). Multiple logistic regression analysis of the whole sample revealed that patients on MS were younger and more likely to be men and to have EPS and a longer duration of illness. Compared to patients in China, those in Japan were more likely to receive MS, while Korean patients were prescribed less MS. In contrast, there were no significant sociodemographic or clinical correlates of BZD use. Compared to patients in China, Korean and Singaporean patients were more likely to be on BZD<sup>52</sup>.
  9. The prescription frequency for low doses of antipsychotic medications (300 mg/day CPZeq or less) in older Asian was 40.9% in the pooled sample. Sixty-five percent was found in the Malaysian sample. Multiple logistic regression analysis of the whole sample showed that patients on low doses of antipsychotic medications were more likely to be female, older, have a shorter length of illness and less positive symptoms. Of patients in the six countries and territories that participated in all the surveys between 2001 and 2009, those in Japan were less likely to receive low doses of antipsychotics<sup>53</sup>.
  10. Prescribing patterns of several FGAs and SGAs medications administered to older Asian patients with schizophrenia during the period between 2001 and 2009 were studied. Of the 467 patients, 192 (41.1%) received FGAs only, 166 (35.5%) received SGAs only and 109 (23.3%) received a combination of FGAs and SGAs. Of the FGAs, haloperidol was the most commonly used (31.3%; mean  $9.4 \pm 6.7$  mg/day), followed by chlorpromazine (15.4%; mean  $126.4 \pm 156.4$  mg/day) and sulpiride (6.6%; mean  $375.0 \pm 287.0$  mg/day). Of the SGAs, risperidone was the most commonly used (31.5%; mean  $4.5 \pm 2.7$  mg/day), followed by olanzapine (13.1%; mean  $13.6 \pm 6.5$  mg/day), quetiapine (7.3%; mean  $325.0 \pm 237.3$  mg/day) and aripiprazole (1.9%; mean  $17.6 \pm 7.7$  mg/day)<sup>54</sup>.
  11. Trends in the use of antidepressants and their demographic and clinical correlates in the treatment of schizophrenia in Asia between 2001 and 2009. The proportion of antidepressant prescription was 6.8% in the whole sample, 5.3% in 2001, 6.5% in 2004 and 8.7% in 2009. There were wide inter-country variations at each survey ranging from 0.9% in Hong Kong to 15.3% in Singapore in 2001; from 1.9% in Korea to 15.4% in Singapore in 2004; and from 2.7% in Japan to 22.0% in Singapore in 2009 and 7% in Malaysia. Multiple logistic regression analysis of the whole sample revealed that patients on antidepressants were younger, more likely to receive benzodiazepines and have significant extrapyramidal side effects and less likely to have significant positive symptoms<sup>55</sup>.
  12. The use of APP in older Asian patients with schizophrenia was studied. The frequency of APP prescription was 51.6% in the pooled sample with wide inter-country variations. Multiple logistic regression analysis of the whole sample showed that patients on APP had higher antipsychotic doses and also were more likely to receive first-generation antipsychotics<sup>56</sup>.
  13. The use of clozapine and its demographic and clinical correlates in older patients with schizophrenia in East Asia during the period between 2001 and 2009 was researched. Clozapine was prescribed for 20.6% of the pooled sample, 19.0% in 2001, 19.4% in 2004 and 22.9% in 2009. Multiple logistic regression analysis of the whole sample revealed that patients taking clozapine had a longer duration of illness, more negative symptoms and were less likely to receive first generation antipsychotic and anticholinergic drugs, but more likely to report weight gain compared to those not receiving clozapine. Compared to those in other sites, older patients in China were more likely to receive clozapine<sup>57</sup>.
  14. The REAP researchers examined the use of high doses of antipsychotic medications ( $\geq 600$ mg/day chlorpromazine equivalent) in older Asian patients with schizophrenia and its demographic and clinical correlates. The frequency for high-dose antipsychotic medications was 36.0% overall, with 38.4% in 2001, 33.3% in 2004 and 36.0% in 2009. Multiple logistic regression analysis of the whole sample showed that compared to patients receiving low-medium antipsychotic doses, those on high doses had a longer illness duration (odds ratio (OR): 2.0, 95% confidence interval (CI): 1.2-3.3,  $p=0.008$ ), were more likely to be in the

50-59 year age group (OR: 0.95, 95% CI: 0.94-0.97,  $p < 0.001$ ), had more often current positive (OR: 1.5, 95% CI: 1.2-1.8,  $p < 0.001$ ) or negative symptoms (OR: 1.3, 95% CI: 1.03-1.6,  $p = 0.03$ ), and more commonly received antipsychotic polypharmacy (OR: 5.3, 95% CI: 4.1-6.7,  $p < 0.001$ ). Extrapyramidal symptoms ( $p = 0.25$ ) and tardive dyskinesia ( $p = 0.92$ ) were not more frequent in the high-dose group<sup>58</sup>.

### Community Psychiatry & Rehabilitation

Hospital-based community psychiatric service has been practiced in Malaysia for several years. Rahima *et al* studied patients with schizophrenia in Kuala Lumpur Hospital who received this service and found 90% of them had low rate of hospital admission with significant reduction in hospitalisation within one year of being enrolled in this service<sup>59</sup>. Among these patients, 74% achieved functional remission and 20% gained employment<sup>60</sup>. In terms of assertive community treatment, good remission outcome (76% remained in remission) was found<sup>61</sup>.

Tan *et al* from UMMC studied patients from Bahagia Hospital, and found that community based patients were significantly less depressed, and had higher functional capability than chronic schizophrenia inpatients<sup>62</sup>. Marhani *et al* from UKM studied the cognitive function of patients with schizophrenia and examined the correlation with employment. The result supported the role of cognitive function, especially attention, working memory and executive function on attaining and maintaining employment in patients with schizophrenia<sup>63</sup>.

### Psychotherapy

Psychoeducation is one of the commonest and most important non-pharmacological treatment of schizophrenia. Paranthaman *et al* from Jelapang Health Clinic provided structured psychoeducation to caregivers in a controlled interventional environment. Caregivers that were given structured psychoeducation showed significant improvement in knowledge, reduced burden in caring for patients and reduced default rate among patients<sup>64</sup>. Ruzanna *et al* from the UKM also established the role of psychoeducation in improving the insight of patients with schizophrenia. It was also found that a shorter duration of illness and having no previous history of admission to mental institution were significantly related to improvement of insight<sup>65</sup>.

Alwi *et al* from USM studied cognitive remediation therapy. They found this therapy to have good prospect as promising preliminary results revealed improvement in cognitive function of patients with schizophrenia<sup>66</sup>. Azhar carried out an open trial using cognitive psychotherapy to treat chronic drug resistant delusion in patients with schizophrenia, and found a positive response in all patients<sup>67</sup>.

### QUALITY OF LIFE AND SOCIAL LIVING

Quality of life has been emphasised in the management of schizophrenia, yet data from developing countries are lacking. Using the data from the NMHR for schizophrenia, the differences in subjective quality of life between FGAs and SGAs was explored. Patients with first-episode schizophrenia and related psychosis were recruited from Kuala Lumpur Hospital. There were no significant statistical differences between groups concerning subjective quality of life, extrapyramidal side effects and employment status at the end of a one-year regular treatment. Significant less benzhexol usage was reported among SGAs ( $P < 0.001$ ) compared to FGAs and sulpiride. Overall, the results are in line with other major pragmatic clinical trials<sup>68</sup>.

Determinants of quality of life in schizophrenia were looked into using the same database from NMHR. Gender, positive and disorganised symptoms of schizophrenia, and cognitive and physical impairments appeared to be the most important predictors of subjective quality of life among the patients from this centre in Malaysia<sup>69</sup>. Mohd Bahli *et al* from the UKM found employment and task-oriented coping style to be positively correlated with better quality of life, while emotion-oriented coping style was not<sup>70</sup>. Hasanah and Razali from USM compared quality of life between patients with diabetes mellitus and schizophrenia who were well controlled with antipsychotics. They found no significant difference in the psychological well-being and level of independence between the two groups. However, it was revealed that the most impaired aspect of well being in the schizophrenia group was social relationship<sup>71</sup>.

Osman *et al* from UKM found 14% of care-givers of schizophrenia patients from Permai Hospital had psychological distress and 6% had depressive disorder. They found significant association between depressive disorders and family functioning dimensions in terms of communication and roles<sup>72</sup>. Both Lua and Zanariah from the Universiti Sultan Zainal Abidin, Terengganu and Ruzanna *et al* from UKM found significantly better quality of life experienced by care givers who were young, male, adequately educated, had regular income, physically healthy and employed<sup>73,74</sup>. Mubarak and Barber from the Flinders University of South Australia studied the quality of life of community-based chronic schizophrenia patients in Penang; and their research showed that emotional involvement of key caregivers significantly improved quality of life<sup>75</sup>.

The patient's capacity to function is another important element in the recovery process of schizophrenia. Norlelawati *et al* from the International Islamic University of Malaysia studied the relationship between psychological symptoms, medications and social demographic and the psychosocial function of schizophrenia patients. They found positive, negative and disorganised symptoms of schizophrenia to be negatively correlated with psychosocial function. Patients treated with FGAs (except sulpiride) had poorer psychosocial function<sup>76</sup>.

### STIGMA & DISCRIMINATION

Many people with schizophrenia experience stigma caused by other people's knowledge, attitudes, and behaviour; and this can lead to impoverishment, social marginalisation, and a low quality of life. As a result, the Department of Psychiatry and Mental Health, Kuala Lumpur Hospital (HKL) collaborated with 26 countries to form the INDIGO network (International Study of Discrimination and Stigma Outcomes). Discrimination was measured with the newly validated discrimination and stigma scale (DISC), which produces three sub scores: positive experienced discrimination; negative experienced discrimination; and anticipated discrimination. Three hundred and forty four (47%) of the 729 participants experienced negative discrimination when they tried making or keeping friends, 315 (43%) of 728 from their family members, 209 (29%) of 724 when finding a job, 215 (29%) of 730 when keeping a job, and 196 (27%) of 724 during intimate or sexual relationships. Positive experienced discrimination was rare. Anticipated discrimination affected 469 (64%) when applying for work, training, or education and 402 (55%) who were looking for a close relationship; 526 (72%) felt the need to conceal their diagnosis. Over a third of participants had anticipated discrimination when seeking a job or during close personal relationships when no discrimination was experienced. From the study, it was obvious the discrimination

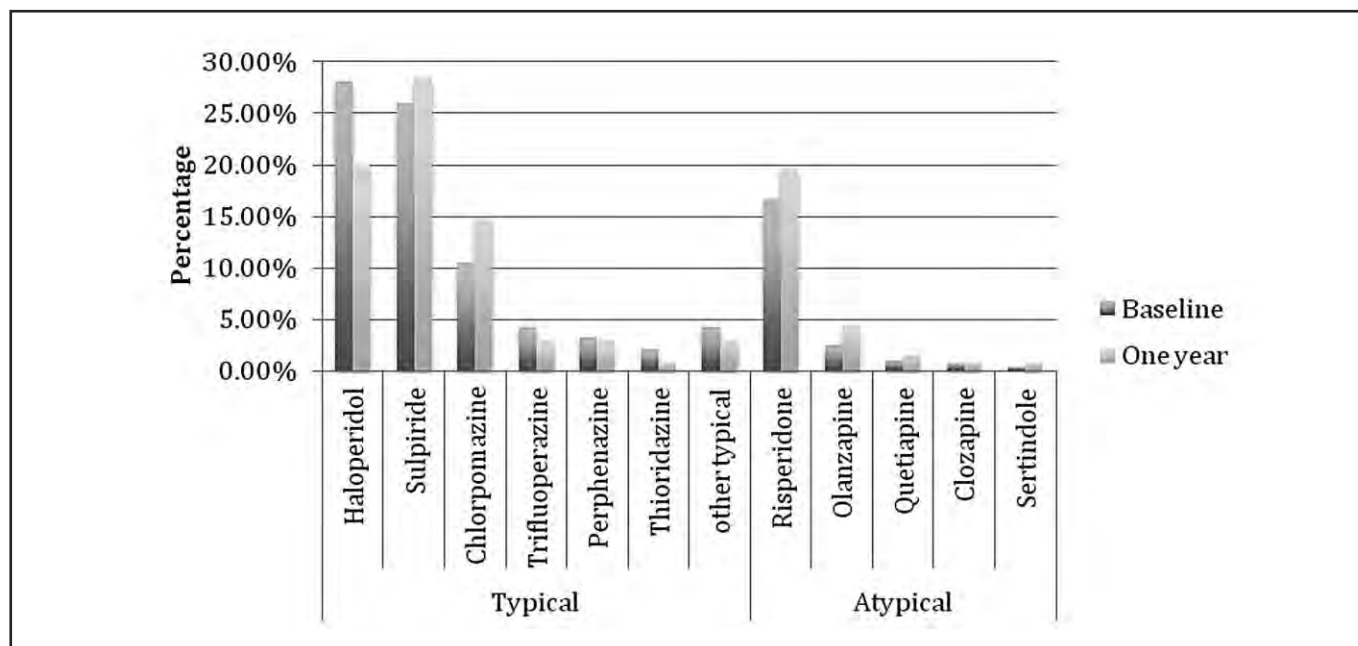


Fig. 1: Comparison of types of antipsychotic medications usage between baseline and at one-year follow-up.

experienced by schizophrenia patients in Malaysia was no different from the rest of the world<sup>77</sup>. Mubarak *et al* from the Flinders University of South Australia studied the quality of life of community-based chronic schizophrenia patients in Penang, Malaysia and found the patients experienced social isolation, discrimination and exploitation at the workplace<sup>78</sup>.

With regards to anticipated discrimination, 64% of the participants reported that they had stopped themselves from applying for work, training or education because of the anticipated discrimination. Many (72%) of them reported that they felt the need to conceal their diagnosis. The expectation of being avoided by others who knew about their diagnosis was highly associated with decisions to conceal their diagnosis. Those who concealed their diagnosis were younger and more educated. The participants who perceived discrimination by others were more likely to stop themselves from looking for a close relationship. Anticipated discrimination in finding and keeping work was more common in the absence than in the presence of experienced discrimination. Similar findings were found for intimate relationships<sup>79</sup>.

Private general practitioners have always been encouraged to manage schizophrenia patients but the response was disappointing. Ahmad Hatim and Hussain Habil from University Malaya Medical Centre (UMMC) looked into this issue and from the 15.6% that responded to the survey, most of them felt they need more training in managing even stable schizophrenia<sup>80</sup>.

## SECTION 2: RELEVANCE OF FINDINGS FOR CLINICAL PRACTICE

Incidence of schizophrenia in Malaysia was reported to be 7.7-43.0 per 100,000 population and majority of them was unemployed. Long DUP (mean 37.6 months) was documented and it was associated with low educational background, the female gender and co-morbidity. Contact with traditional

healer was common but not associated with treatment delay. On the contrary, ignorance of illness by patient and family member was the main reason for the delay. Substance-use comorbidity was commonly found among people with schizophrenia.

High rate of treatment discontinuation was found after one year of treatment and weight gain and metabolic syndrome were the major adverse events for those who were on treatment, particularly SGAs. Majority of the patients had insulin resistance. Frequency of TD was low compared to the other Asia countries. Twelve percent of patients reported sexual dysfunction.

Almost half of the patients received more than one antipsychotic medication. Although the use of anticholinergic medication declined over the years, there was still a substantial amount of such prescription among the elderly patients. Community psychiatric service had shown definite benefit in terms of reducing hospitalisations, improving remission outcome, and increasing functional capability and employment.

Different domains of self-rated quality of life correlated with different sociodemographic and clinical characteristics. Some of the characteristics were malleable such as positive symptoms of schizophrenia and depressive illness. Stigma and discrimination were still prevalent among the patients and most of them would conceal their diagnosis from employers. There were no significant difference between Malaysia and other parts of the world with regards to anticipated and experienced discrimination by the patients with schizophrenia.

## SECTION 3: FUTURE RESEARCH DIRECTION

After 10 years of schizophrenia research in Malaysia, the time has come to shift from merely presenting local data to establishing hypothesis. There is a lot of replication of studies mostly done in treatment and clinical areas. There also seems



to be a lack of research in basic science involving genetics and other biological areas. In Malaysia presently, there is a need for more research that examines the relationships among genetic, neuroimaging (functional and structural), behavioral, developmental, social, and other factors in greater depth. This is important to understand the causes of the disorder and how it can be predicted and prevented.

The constraints that researchers in Malaysia face are numerous. The lack of resources, lack of research interest among psychiatrists and overwhelming clinical work are just some of the challenges. Another major factor is the over-emphasis in industrial-initiated studies by some centres including universities; thus resulting in less effort on investigator-initiated studies. A concerted effort by the Ministry of Health and the Universities is needed to meet this demand through research initiatives. Collaboration among centres may be one of the ways to overcome limited resources within a single centre. In the past, universities have been carrying out research in Ministry of Health hospitals due to the fact that these hospitals have more types of illnesses and more patients. For more meaningful collaborations, the previous practice of not getting Ministry of Health teams actively involved in research or as co-authors should be remedied.

Despite the availability of government funding, there were few takers by the Mental Health Services in the Ministry of Health. This is partly due to the lack of awareness and the reluctance to put in the effort in securing the grant.

In the long term, research in this area can be stimulated through the combined efforts of all involved with each complimenting the other. For more fruitful research, we have to move from merely presenting some data from a single hospital to conducting research that can be translated into clinical practice. It is hoped, that we can utilise available resources to be the world renowned research centre in schizophrenia.

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