Neuropsychiatric Disease and Treatment

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

The Prevalence of Tardive Dyskinesia In Patients With Schizophrenia Treated With Antipsychotics In Malaysia

Anbumalar Nedunjelian*, Chong Guan Ng*, Poh Khuen Lim*, Ahmad Hatim Sulaiman, Ong Hui Koh, Benedict Francis

The Department of Psychological Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

*These authors contributed equally to this work

Correspondence: Chong Guan Ng, The Department of Psychological Medicine, University of Malaya, Kuala Lumpur, Federal Territory of Kuala Lumpur, 50603, Malaysia, Email chong_guan@um.edu.my

Background: Tardive dyskinesia (TD) is a movement disorder that is associated with the prolonged use of antipsychotics. The prevalence of TD varies widely from 20% to 50% but often undetected in schizophrenia patients treated with antipsychotics.

Aim: This study is aimed at investigating the prevalence of TD among schizophrenia patients treated with antipsychotics and identifying the associated factors. This study also investigates the association of TD with personal and social functioning performance, and the severity of illness.

Methods: This was a cross-sectional study conducted at a teaching hospital in Malaysia. Patients were assessed using the Abnormal Involuntary Movement Scale (AIMS), Personal and Social Performance Scale (PSP) and the Clinical Global Impression Scale (CGI).

Results: Seventy-eight patients were recruited in this study. The prevalence of TD was 35.9%. Older age (OR 4.079, p = 0.006), Chinese ethnicity (OR 4.486, p = 0.020), longer duration of schizophrenia and antipsychotic treatment (OR 5.312, p = 0.001 and OR 5.500, p = 0.002 respectively) were also significantly associated with TD. TD patients notably demonstrated severe impairments in the self-care domain (71.4%). The presence of TD is associated with more severe overall clinical impairment (53.6%).

Conclusion: TD remains a prevalent and concerning side effect of antipsychotic treatment in schizophrenia patients. There is a need for regular monitoring and the use of standardized assessment tools to detect TD.

Keywords: tardive dyskinesia, schizophrenia, antipsychotics, movement disorders

Introduction

Tardive dyskinesia (TD) is thought to arise from prolonged exposure to dopamine receptor-blocking agents, especially antipsychotics. The most widely accepted theory is dopaminergic hypersensitivity, which suggests that chronic blockade of D2 receptors leads to their upregulation and hypersensitivity. This compensatory mechanism may result in abnormal, involuntary movements when dopamine signalling becomes excessively active in these hypersensitized pathways.[1,2]

Another contributing mechanism is oxidative stress, which postulates that long-term antipsychotic use generates excessive reactive oxygen species. This oxidative damage, particularly in the basal ganglia, can lead to neuronal injury and functional dysregulation in motor control areas. Patients with comorbid conditions such as diabetes and older adults may be more vulnerable due to compromised antioxidant defenses and pre-existing neural vulnerabilities.[3,4]

GABAergic dysfunction is also implicated in TD. The basal ganglia rely on gamma-aminobutyric acid (GABA) for inhibitory control, and reductions in GABAergic activity could disrupt the delicate balance between excitation and inhibition, leading to the motor symptoms seen in TD.[5] Similarly, neuroplastic changes, including maladaptive synaptic remodelling and altered neuronal connectivity due to chronic drug exposure, may further exacerbate movement abnormalities.[6]

Received: 11 October 2024
Accepted: 21 December 2024
Published: 5 March 2025

Furthermore, metabolic and cerebrovascular contributions have been recognized as potential risk factors. Older adults and patients with cerebrovascular insults or diabetes may exhibit increased susceptibility to TD due to pre-existing vulnerabilities in motor pathways combined with dopaminergic dysregulation.[7,8] Additionally, genetic and epigenetic factors such as variations in dopamine receptor genes (eg, DRD2) or epigenetic modifications due to chronic antipsychotic exposure may also influence individual susceptibility to TD.[9]

TD is a distressing and often irreversible movement disorder predominantly associated with the prolonged use of antipsychotic medications. This condition is characterized by repetitive, involuntary, and nonrhythmic movements, primarily affecting the orofacial region but can also involve the limbs and trunk.[10] TD can profoundly impact patients' quality of life, leading to social stigmatization, emotional distress, and functional disability. The hallmark of TD is its delayed onset relative to the initiation of antipsychotic therapy, typically emerging after months or years of continuous medication use.[11]

Several risk factors have been identified for the development of TD, including patient demographics, duration and dose of antipsychotic treatment, genetic factors, and medical comorbidities. Age is a significant risk factor for TD, with older patients exhibiting a higher susceptibility. Jeste and Caligiuri[12] found that elderly patients have a two- to three-fold increased risk of developing TD compared to younger adults. This increased risk may be attributed to age-related changes in brain structure and function, as well as increased sensitivity to medications.

The prevalence of TD among schizophrenia patients varies widely, with estimates ranging from 13% to 32% across studies due to differences in study populations, diagnostic criteria, and methodologies.[13] Recent studies provide a more nuanced understanding of the prevalence of TD globally. For instance, a meta-analysis by Carbon et al[14] reported a pooled prevalence of TD of 25.3% among patients treated with first-generation antipsychotics and 13.1% among those treated with second-generation antipsychotics.

In Asia, the prevalence of TD among schizophrenia patients presents unique epidemiological insights due to diverse genetic, environmental, and treatment-related factors. A study conducted in Singapore by Chong[6] found that the prevalence of TD was 40.6% for Chinese patients and 29.0% for Malay patients. Significant risk factors for TD included advanced age and lower current antipsychotic dosage. Adjusted analyses showed no significant difference in TD prevalence between ethnic groups, suggesting that medication practices may play a larger role than genetic factors. A comprehensive study conducted in China by Zhang et al[15] found that the prevalence of TD was 24.2% among patients on long-term antipsychotic treatment. The study highlighted that patients treated with first-generation antipsychotics had a significantly higher risk compared to those on second-generation medications.

TD can severely impair a patient's ability to engage in socially useful activities, particularly employment. A study by Caroff et al[16] found that individuals with TD were less likely to be employed and, when employed, often faced difficulties in job performance due to the physical manifestations of the disorder. Patients may also experience social withdrawal and isolation as a result of the negative reactions from others to their involuntary movements. Mentzel et al[17] highlighted that social stigma associated with TD exacerbates the social deficits inherent in schizophrenia, leading to further deterioration in personal relationships and the ability to engage in social activities. Patients with TD often experience stigmatization, social withdrawal, and reduced quality of life, which can exacerbate the underlying psychiatric condition.[18] Therefore, balancing the therapeutic benefits of antipsychotic medications with their potential adverse effects is crucial in the treatment of schizophrenia.

This study aimed to investigate the prevalence of TD in schizophrenia patients treated with antipsychotics and its associated sociodemographic risk factors. This study also explored the impact of TD on a patient's personal and social performance and the association of TD with the illness severity of schizophrenia.

Materials and Methods

Study Design and Setting

This is a cross-sectional study. This study was conducted from March 2024 to May 2024 at University Malaya Medical Centre, a university hospital located in Kuala Lumpur, Malaysia. The sample size was estimated using the following formula: $n = t2x\frac{p(1-p)}{m2}$.[19]

Hence, the calculated estimated sample size was 70.

Patients

A total of 78 patients who were diagnosed with schizophrenia using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and were on antipsychotics were recruited into this study using a convenience sampling method. All the patients were recruited from the inpatient and the outpatient services of the Department of Psychological Medicine, University Malaya Medical Centre.

The inclusion criteria of this study were patients i) aged 18 years and above, ii) diagnosed with Schizophrenia according to the DSM-5 criteria, iii) undergoing treatment with antipsychotics for at least a period of 12 months. Exclusion criteria were patients who were i) diagnosed to have psychotic disorder secondary to organic cause such as Parkinson's Disease, epilepsy or stroke; ii) diagnosed with TD secondary to neurological causes; iii) diagnosed with organic disorders that could cause movement disorders. Written consent was obtained from patients who were recruited in this study. All patients were literate in the English or Malay language. All participants were informed about the purpose of the study.

Ethics approval was granted by the Medical Research Ethics Committee, University Malaya Medical Centre (MREC ID NO: 2024112–13,235). This study complies with the Declaration of Helsinki.

Instruments

Sociodemographic Questionnaire

Sociodemographic information was collected through self-report questionnaires which included age, gender, marital status, race, education level, and employment status.

Additional clinical information was gathered which included the duration of schizophrenia diagnosis, duration of antipsychotic treatment, current antipsychotics and doses, previous antipsychotic medications, history of past admissions, history of receiving electroconvulsive therapy, comorbid psychiatric diagnosis, family history of schizophrenia, medical conditions, concomitant medications besides antipsychotics, and lifestyle factors such as smoking, alcohol consumption and illicit drug use.

The Abnormal Involuntary Movement Scale (AIMS)

The Abnormal Involuntary Movement Scale (AIMS) is a critical diagnostic tool for the assessment of involuntary movements, which are often associated with the long-term use of antipsychotic medications.[10] The AIMS encompasses a 12-item scale that assesses various dimensions of involuntary movements, including facial and oral movements, extremity and trunk movements, and global judgments related to the overall severity of symptoms, incapacitation, and patient awareness of the abnormal movements. These items are rated on a five-point scale of severity from 0 to 4. The scale is rated from 0 (none), 1 (minimal), 2 (mild), 3 (moderate), 4 (severe).

The Schooler-Kane criteria are commonly employed for research diagnoses of TD.[20] In our study, the Schooler-Kane criteria was used as a research tool rather than a definitive diagnostic standard. Based on the Schooler-Kane criteria, the presence of at least "moderate" abnormal involuntary movements in one or more body areas or at least "mild" movements in two or more body areas (face, lips, jaw, tongue, upper extremities, lower extremities, trunk) which given a rating of 2 or higher on the AIMS scale, is evidence of tardive dyskinesia. If the patient has mild TD in two areas or moderate movements in one area, then he or she should be given a diagnosis of TD. The Schooler-Kane criteria are research-oriented and not mandatory for clinical diagnosis.

The clinical diagnosis of TD should prioritize any observable abnormal movements and their impact on daily functioning. Treatment should be driven by the functional impairments caused by these movements rather than the severity of movements alone.

The Personal and Social Performance Scale (PSP)

The Personal and Social Performance (PSP) Scale is an instrument designed to assess the social functioning of individuals with severe mental disorders, particularly schizophrenia.[12] It focuses on four critical domains: socially useful activities, personal and social relationships, self-care, and disturbing and aggressive behaviours.

The scale ranges from 1 to 100, with higher scores indicating better functioning. It is divided into ten equal intervals, each describing different levels of impairment and corresponding behavioural examples, facilitating the accurate rating of

a patient's abilities and challenges. By focusing on observable behaviours and performance, the PSP provides a more objective assessment compared to self-report measures.

The Clinical Global Impression (CGI)

The Clinical Global Impression (CGI) Scale is a widely used, clinician-rated instrument designed to assess treatment response and the overall severity of mental illness. The component used in this study is the "CGI-Severity (CGI-S)" which assesses the current severity of the patient's illness on a seven-point scale, ranging from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). This rating is based on the clinician's overall impression of the patient's condition at the time of assessment.

Statistical Analysis

The data analyses for this study were performed using the Statistical Package for the Social Sciences (SPSS) version 29 (IBM Corp., Armonk, NY). Descriptive analysis was used to report the prevalence of TD among schizophrenia patients treated with antipsychotics at. The analysis included socio-demographic and clinical characteristics, medication-related factors, as well as instruments of PSP and CGI. Descriptive analysis included means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Statistical significance was assessed using a p-value threshold of less than 0.05.

Logistic regression analysis was applied to explore the relationship between various socio-demographic and clinical characteristics, as well as medication use, with the prevalence of TD. Additionally, logistic regression was conducted to determine the association between these characteristics and the domains of the Personal and Social Performance (PSP) scale and the Clinical Global Impression (CGI) scale.

Initially, simple logistic regression was conducted to estimate the crude odds ratio (COR) and its 95% confidence interval (CI). Variables significant at a p-value of 0.05 or less were entered into the multiple logistic regression model to estimate the adjusted odds ratio (AOR) and its 95% CI, with a p-value of less than 0.05 considered significant. Model fitness was assessed using the Hosmer–Lemeshow goodness-of-fit test, with a p-value of more than 0.05 considered indicative of a good fit.

Results

Among the 78 patients, there were more females (57.7%) compared to males (42.3%). The average age of patients was 46.4 years (Table 1). Majority of the patients were Chinese (44.9%), followed by Malays (29.5%) and Indians (21.8%). Most patients having completed secondary education (56.4%), and majority of the patients were unemployed (70.5%).

The duration of schizophrenia among patients had a mean of 18.8 years. Similarly, the duration of antipsychotic treatment had a mean of 18.7 years. A substantial proportion of patients (78.2%) had a history of psychiatric ward admission, with a mean duration of 4.81 years.

In this study, the prevalence of TD was 35.9% (n=28).

Table 1 Socio Demographic and Clinical Characteristics of Schizophrenia Patients Treated With Antipsychotics

Socio Demographic and clinical characteristics	Non-TD (%) (n= 50) (64.1)	TD (%) (n= 28) (35.9)	Total 78 (100.0)
Gender			
Male	31 (62.0)	14 (50.0)	45 (57.7)
Female	19 (38.0)	14 (50.0)	33 (42.3)
Age			
18–45 years old	31 (62.0)	8 (28.6)	39 (50.0)
46 years old and above	19 (38.0)	20 (71.4)	39 (50.0)

(*Continued*)

Table 1 (Continued).

Socio Demographic and clinical characteristics	Non-TD (%) (n= 50) (64.1)	TD (%) (n= 28) (35.9)	Total 78 (100.0)
Race			
Malay	19 (38.0)	4 (14.3)	23 (29.5)
Chinese	18 (36.0)	17 (60.7)	35 (44.9)
Indian	11 (22.0)	6 (21.4)	17 (21.8)
Others	2 (4.0)	1 (3.6)	3 (3.8)
Education level			
Primary	12 (24.0)	7 (25.0)	19 (24.4)
Secondary	27 (54.0)	17 (60.7)	44 (56.4)
Tertiary	11 (22.0)	4 (14.3)	15 (19.2)
Employment status			
Employed	13 (26.0)	4 (14.3)	17 (21.8)
Others	37 (74.0)	24 (85.7)	61 (78.2)
Unemployed	35 (70.0)	20 (71.4)	55 (70.5)
Retired		4 (14.3)	4 (5.1)
Student	2 (4.0)		2 (2.6)
Duration of Schizophrenia (years)			
1–18 years	34 (68.0)	8 (28.6)	42 (53.8)
18 years and above	16 (32.0)	20 (71.4)	36 (46.2)
Duration of Antipsychotic (years)			
1–17 years	30 (60.0)	6 (21.4)	36 (46.2)
17 years and above	20 (40.0)	22 (78.6)	42 (53.8)
History of admission to psychiatric ward			
No	7 (14.0)	2 (7.1)	9 (11.5)
Yes	43 (86.0)	26 (92.9)	69 (88.5)
Smoking			
No	30 (60.0)	21 (75.0)	51 (65.4)
Yes	20 (40.0)	7 (25.0)	27 (34.6)
Alcohol			
No	39 (78.0)	25 (89.3)	64 (82.1)
Yes	11 (22.0)	3 (10.7)	14 (17.9)
Illicit substance abuse			
No	37 (74.0)	26 (92.9)	63 (80.8)
Yes	13 (26.0)	2 (7.1)	15 (19.2)
Cannabis			
No	42 (84.0)	27 (96.4)	69 (88.5)
Yes	8 (16.0)	1 (3.6)	9 (11.5)
Methamphetamine			
No	45 (90.0)	28 (100.0)	73 (93.6)
Yes	5 (10.0)		5 (6.4)
Others			
No	46 (92.0)	27 (96.4)	73 (93.6)
Yes	4 (8.0)	1 (3.6)	5 (6.4)

https://doi.org/10.2147/NDT.S494458

Table 2 displays the outcome measures for schizophrenia patients with TD treated with antipsychotics, evaluated using the Abnormal Involuntary Movement Scale (AIMS), the Personal and Social Performance Scale (PSP), and the Clinical Global Impression (CGI). The data shows that facial and oral movements were predominantly mild, affecting 50.0% of patients, followed by minimal movements in 28.6%, moderate movements in 17.9%, and severe movements in 3.6% of patients. For extremity movements, 42.9% of patients experienced minimal severity, 39.3% had mild movements, and 17.9% had no extremity movements. Regarding trunk movements, 60.7% of patients had no trunk movements, while the remaining 39.3% experienced minimal movements.

The PSP indicated that 85.7% of patients had very severe impairments in socially useful activities, including work and study, as well as in personal and social relationships. Self-care was severely affected in 71.4% of patients, while 28.6% showed mild or absent impairments. Disturbing and aggressive behaviors were generally mild or absent in 92.9% of patients, with only 7.1% experiencing very severe behaviors.

The CGI scale evaluates the overall severity of illness. According to the CGI, over half of the patients (53.6%) were considered moderately ill or worse, while 46.4% were mildly ill or better.

Table 2 Outcome Measures of Schizophrenia Patients Who Exhibited TD (n=28) Treated With Antipsychotics

Outcome Measures	**n (%)**
Abnormal involuntary movement scale (AIMS)	
Facial and oral movements	
Minimal	8 (28.6)
Mild	14 (50.0)
Moderate	5 (17.9)
Severe	1 (3.6)
Extremity movements	
None	5 (17.9)
Minimal	12 (42.9)
Mild	11 (39.3)
Trunk movements	
None	17 (60.7)
Minimal	11 (39.3)
Personal & social performance scale (PSP)	
Socially useful activities, work, study	
Absent – mild	4 (14.3)
Manifest – very severe	24 (85.7)
Personal and social relationships	
Absent – mild	4 (14.3)
Manifest – very severe	24 (85.7)
Self-care	
Absent – mild	8 (28.6)
Manifest – very severe	20 (71.4)
Disturbing and aggressive behaviors	
Absent – mild	26 (92.9)
Manifest – very severe	2 (7.1)
Clinical global impression (CGI)	
Severity of illness	
Mildly ill and below	13 (46.4)
Moderate ill and above	15 (53.6)

Table 3 demonstrates the associations between sociodemographic, clinical characteristics and TD. In the univariate analysis, several factors showed significant associations with TD, namely older age (>46 years), Chinese ethnicity, longer durations of schizophrenia (>19 years) and antipsychotic treatment (>18 years).

In the multivariate analysis adjusting for potential confounders, the duration of antipsychotic treatment (>18 years) remained statistically significant and independently associated with TD (AOR 3.560, p = 0.017). Chinese ethnicity also maintained a significant association with TD in the multivariate model (AOR 4.888, p = 0.025). The Hosmer–Lemeshow goodness-of-fit test confirmed a good fit for the multiple logistic regression model (p = 0.953), indicating that the model effectively explains the relationship between various socio-demographic and clinical characteristics and the prevalence of TD among schizophrenia patients.

Table 4 demonstrates the correlation of sociodemographic and clinical factors with the severity of self-care impairments. Univariate analysis showed that the presence of TD had a significant association with the severity of self-care impairments (OR 3.182, p = 0.022; AOR 3.340, p = 0.025).

Table 3 Associations Between Socio-Demographic and Clinical Characteristics and the Prevalence of TD Among Schizophrenia Patients Treated With Antipsychotics

Socio Demographic and Clinical Characteristics	non-TD (n = 50)	TD (n = 28)	COR (95% CI) [A]	p value	AOR (95% CI)[B]	p value
Gender						
Male	31 (62.0)	14 (50.0)				
Female	19 (38.0)	14 (50.0)	1.632 (0.640, 4.157)	0.305		
Age						
18–45 years old	31 (62.0)	8 (28.6)				
46 years old and above	19 (38.0)	20 (71.4)	4.079 (1.502, 11.079)	0.006*	1.887 (0.574, 6.202)	0.296
Race						
Malay	19 (38.0)	4 (14.3)				
Chinese	18 (36.0)	17 (60.7)	4.486 (1.265, 15.905)	0.020*	4.888 (1.218, 19.621)	0.025*
Indian	11 (22.0)	6 (21.4)	2.591 (0.598, 11.234)	0.203	3.131 (0.610, 16.068)	0.171
Others	2 (4.0)	1 (3.6)	2.375 (0.171, 32.999)	0.519	3.975 (0.189, 83.465)	0.374
Education level						
Primary	12 (24.0)	7 (25.0)				
Secondary	27 (54.0)	17 (60.7)	1.079 (0.355, 3.283)	0.893		
Tertiary	11 (22.0)	4 (14.3)	0.623 (0.142, 2.727)	0.530		
Employment status						
Employed	13 (26.0)	4 (14.3)				
Unemployed	37 (74.0)	24 (85.7)	2.108 (0.614, 7.232)	0.236		
Duration of Schizophrenia (years)						
1–18 years	34 (68.0)	8 (28.6)				
19 years and above	16 (32.0)	20 (71.4)	5.312 (1.930, 14.624)	0.001**	1.515 (0.260, 8.833)	0.644
Duration of Antipsychotic (years)						
1–17 years	30 (60.0)	6 (21.4)				
18 years and above	20 (40.0)	22 (78.6)	5.500 (1.895, 15.960)	0.002**	3.560 (0.575, 22.026)	0.017*
Smoking						
No	30 (60.0)	21 (75.0)				
Yes	20 (40.0)	7 (25.0)	0.500 (0.179, 1.394)	0.185		
Alcohol						
No	39 (78.0)	25 (89.3)				
Yes	11 (22.0)	3 (10.7)	0.425 (0.108, 1.677)	0.222		

(*Continued*)

https://doi.org/10.2147/NDT.S494458

Table 3 (Continued).

Socio Demographic and Clinical Characteristics	non-TD (n = 50)	TD (n = 28)	COR (95% CI) [A]	p value	AOR (95% CI)[B]	p value
Illicit substance abuse						
No	37 (74.0)	26 (92.9)				
Yes	13 (26.0)	2 (7.1)	0.219 (0.046, 1.053)	0.058		
Cannabis						
No	42 (84.0)	27 (96.4)				
Yes	8 (16.0)	1 (3.6)	0.194 (0.023, 1.643)	0.133		
Methamphetamine						
No	45 (90.0)	28 (100.0)				
Yes	5 (10.0)					
Others						
No	46 (92.0)	27 (96.4)				
Yes	4 (8.0)	1 (3.6)	0.426 (0.045, 4.010)	0.456		
Antipsychotic						
First generation and combination	17 (34.0)	10 (35.7)				
Second generation	33 (66.0)	18 (64.3)	0.927 (0.352, 2.445)	0.879		

Notes: *Significant at p<0.05. [A]COR estimates from simple logistic regression. [B]AOR estimates from multiple logistic regression; assumptions of logistic regression have been met and the Hosmer-Lemeshow goodness-of-fit test indicated good fit (p=0.953). Analyses were adjusted for age, race, duration of schizophrenia and duration of antipsychotic.

Table 4 Associations Between Socio-Demographic and Clinical Characteristics With the Severity of Self-Care Impairments Among Schizophrenia Patients Treated With Antipsychotics

Socio demographic	Absent – mild (n=63)	Manifest –Very severe (n=15)	COR (95% CI) [A]	p value	AOR (95% CI) [B]	p value
TD						
No	28 (77.8)	22 (52.4)				
Yes	8 (22.2)	20 (47.6)	3.182 (1.180, 8.580)	0.022*	3.340 (1.162, 9.599)	0.025*

Notes: *Significant at p<0.05. [A]COR estimates from simple logistic regression. [B]AOR estimates from multiple logistic regression; assumptions of logistic regression have been met and the Hosmer–Lemeshow goodness-of-fit test indicated good fit (p=0.657).

In the multivariate analysis, TD remained a strong predictor, with those affected being 3.34 times more likely to experience severe difficulties in self-care activities compared to those without TD, TD did not show significant association with other three domains in PSP which include socially useful activities, personal and social relationships, disturbing and aggressive behaviours.

Analysis revealed that tardive dyskinesia did not show significant associations with CGI severity.

Discussion

Our study examined the prevalence of Tardive Dyskinesia (TD) among schizophrenia patients treated with antipsychotics. The prevalence of TD was 35.9%. Several studies have demonstrated variable rates of TD, typically ranging between 20% and 50%, which are influenced by factors such as the type of antipsychotics used, duration of treatment, patient age, and underlying genetic predispositions.[2,13] This underscores the necessity for regular monitoring of TD symptoms in schizophrenia patients, especially those on prolonged antipsychotic therapy.[14]

In our study, older age emerged as a significant risk factor, with patients aged 46 years and above showing a substantially higher prevalence of TD. Age is one of the most consistently established risk factors identified for the development of TD.[15–19] This may be attributed to higher-age-related degenerative effects in the (dopaminergic) nigrostriatal system, and the lack of readily exhibited neuronal sprouting with subsequent D2 downregulation in the elderly.[18] Additionally, older patients are also more likely to develop diabetes mellitus and cerebrovascular insults, which may in part account for the increased vulnerability for TD.[21] Aging is also associated with less efficient metabolism and

excretion of drugs, and these age-related pharmacokinetic changes may lead to exposure to higher blood levels of antipsychotic medications.[3] This finding is consistent with the literature indicating that prolonged exposure to antipsychotics and age-related susceptibility to movement disorders increase the risk of developing TD.[2,20]

In our study, ethnicity played a crucial role, with Chinese patients exhibiting the highest TD prevalence. Our findings demonstrated that Chinese ethnicity was significantly associated with a higher risk of TD, even after adjusting for other covariates in the multivariate analysis. This finding is particularly notable given the multi-ethnic composition of Malaysia, where ethnic and genetic factors may play a critical role in the development of TD. Previous studies in other populations have suggested genetic predispositions and metabolic differences across ethnic groups as contributing factors, but limited research has specifically explored these associations in Southeast Asian populations. Our study highlights the need for further investigation into ethnicity-specific mechanisms and risk factors, which could inform personalized monitoring and management strategies for TD.

A study conducted in Singapore by Chong[6] reported higher prevalence of tardive dyskinesia (TD) in schizophrenia patients of Chinese ethnicity (40.6%) compared to patients of Malay ethnicity (29.0%). However, the study concluded that there were no significant differences in TD prevalence between Chinese and Malay patients after adjusting for variables such as age, duration of antipsychotic exposure, and extrapyramidal symptoms. This suggests that any observed variation in TD prevalence is likely due to environmental factors, including medication practices, rather than inherent ethnic or genetic differences.

In a review of studies from 15 different countries involving 33,000 antipsychotic treated patients, Kane et al[22] found wide variation in TD rates among countries. Yassa and Jeste[12] noted that across studies undertaken in four continents reviewed by them, the lowest prevalence of TD was reported from Asia. Suggested lower prevalence rates of TD among Chinese subjects from these studies, when compared to studies in Western subjects, have led to the suggestion of inter-ethnic differences, possibly genetic, causing vulnerability to developing TD.[23] A contrary view was expressed by Pi et al,[2] who established differing prevalence rates of TD among Chinese patients in Beijing, China (8.2%), Hong Kong (19.4%), and Yanji, China (18.6%), leading to the suggestion that environmental factors, such as differing prescribing patterns, are more likely to account for any such differences.

Besides age and ethnicity, longer durations of illness and the use of antipsychotic treatment were strongly associated with higher TD prevalence. This supports the hypothesis that the cumulative dose and duration of antipsychotic exposure are critical factors in TD development.[13,24] Addressing these factors in clinical practice through the adoption of lowest effective dose strategies, regular screenings for extrapyramidal symptoms, and considering newer antipsychotics with a lower TD risk profile could be beneficial. Moreover, history of psychiatric ward admissions and electroconvulsive therapy (ECT) were found to be more common among patients with TD, suggesting that these factors might contribute to the development of TD or reflect more severe underlying psychiatric conditions.[25]

Although our study did not find a significant difference in TD prevalence between patients treated with first-generation antipsychotics (FGA) and second-generation antipsychotics (SGA), the high prevalence of TD among patients using haloperidol and chlorpromazine indicates the need for careful monitoring and judicious use of these medications. This finding further stresses the importance that clinicians should consider the risk of TD when prescribing FGAs and explore alternative treatments or adjunctive therapies that might mitigate this risk. Regular assessment using tools such as the Abnormal Involuntary Movement Scale (AIMS) is crucial for early detection and management of TD.[3]

In terms of the abnormal movement, facial and oral movements were the most commonly affected areas, indicating that these areas are particularly susceptible to TD-related motor disruptions. These findings align with existing literature suggesting that facial and oral regions are often the first and most affected sites in TD, potentially due to the high density of dopamine receptors in these regions.[2] Extremity movements showed a mixed severity, with a notable proportion of patients exhibiting involuntary movements. This finding highlights the need for comprehensive motor assessments in patients with TD, as extremity involvement can significantly affect daily functioning and quality of life.[13] Trunk involvement is less common in TD compared to facial, oral, and extremity movements. The relative sparing of the trunk in TD could be due to the lower density of dopamine receptors in these areas or differences in motor control mechanisms.[24]

In regards to the Personal and Social Performance (PSP) Scale, TD patients demonstrated very severe impairments in the self-care domain, indicating significant challenges in performing basic daily activities. This level of impairment

necessitates extensive support and intervention to help patients manage their daily routines and maintain an acceptable quality of life. The burden of self-care deficits on caregivers and healthcare systems is substantial, emphasizing the need for targeted support services and interventions.[13]

In our study, we found that TD patients were more likely to demonstrate moderately ill or worse score on the CGI-S scale, suggesting that the presence of TD is associated with more severe overall clinical impairment. These findings align with previous research that has documented the profound impact of TD on patients' functional abilities and overall quality of life.[2] TD is known to exacerbate the severity of schizophrenia, contributing to higher levels of clinical impairment and disability.[2] This highlights the need for comprehensive management strategies that address both the motor symptoms of TD and the overall clinical severity of schizophrenia.

This study has several limitations. One of the main limitations of this study is its cross-sectional study design, which cannot examine the causal relationship between the variables and also does not allow the assessment of persistent TD. Secondly, the lack of information on previous antipsychotic burden and the presence or absence of movement disorders prior to switching from FGA to SGA is another limitation of our study. Lastly, the small sample size, non-randomization method and the study being conducted in only one setting also posed as limitations. Further studies need to be conducted with other study designs, such as a cohort study, to measure the strength of the study findings.

Conclusion

This study provides an understanding of the prevalence and associated factors of TD in schizophrenia patients treated with antipsychotics. The findings underscore the importance of personalized treatment strategies that consider individual risk factors such as age, ethnicity, socio-economic status, and treatment duration. Clinicians should be particularly vigilant in monitoring older patients and those with prolonged treatment histories to mitigate the risk of TD and ensure optimal patient outcomes. Our study reinforces the importance of routine monitoring and assessment of TD in all patients treated with dopamine-blocking agents, particularly those with established risk factors such as advanced age, prolonged antipsychotic use, and Chinese ethnicity. While these recommendations align with existing guidelines, they hold relevance for the Malaysian population, where ethnicity-specific and regional data remain scarce. Future research should aim to explore the underlying mechanisms driving these associations and to develop tailored intervention strategies to improve the quality of care for diverse populations.

Further research is also needed to evaluate the long-term efficacy and safety SGA concerning TD. Additionally, exploring novel preventative strategies, such as the use of VMAT2 inhibitors or other pharmacological interventions, could offer new avenues for reducing the incidence of TD among patients receiving antipsychotic treatment.[2] Future research should focus on genetic predispositions, novel preventative strategies, and the long-term management of TD to improve patient outcomes and quality of life.

Abbreviations

TD, tardive dyskinesia; AIMS, abnormal involuntary movement scale; PSP, personal and social performance scale; CGI, clinical global impression; FGA, first-generation antipsychotics; SGA, second-generation antipsychotics.

Ethics Approval

All participants were informed about the purpose of the study. Ethics approval was granted by the Medical Research Ethics Committee, University Malaya Medical Centre (MREC ID NO: 2024112-13235). This study complies with the Declaration of Helsinki. This study complies with the Declaration of Helsinki.

Acknowledgment

Anbumalar Nedunjelian, Ng Chong Guan and Lim Poh Khuen, contributed equally to this work and share first authorship.

Disclosure

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Smith JM, Baldessarini RJ. Changes in prevalence, severity, and recovery in tardive dyskinesia with age. *Arch Gen Psychiatry*. 1980;37(12):1368–1373. doi:10.1001/archpsyc.1980.01780250054006
2. Kane JM, Smith JM. Tardive dyskinesia: prevalence and risk factors. *Arch Gen Psychiatry*. 1982;39(4):473–481. doi:10.1001/archpsyc.1982.04290040031004
3. Jeste DV, Wyatt RJ. Understanding and treating tardive dyskinesia. *J Clin Psychiatry*. 1982;43(12):15–21.
4. Woerner MG, et al. Factors predicting the development of tardive dyskinesia. *J Clin Psychopharmacol*. 1998;18(1):42–47. doi:10.1097/00004714-199802000-00008
5. Bhatia KP, et al. Tardive syndromes: phenomenology, pathophysiology, and management. *Lancet Neurol*. 2004;3(7):419–429. doi:10.1016/S1474-4422(04)00851-6
6. Chong SA. Risk factors for tardive dyskinesia among Asian patients with schizophrenia. Doctor of Medicine thesis. National University of Singapore; 2005.
7. Solmi M, et al. Age-related tardive dyskinesia risk in recent meta-analyses. *Psychopharmacol Bull*. 2018;48(3):11–14.
8. Jeste DV, Caligiuri MP. Tardive dyskinesia: role of aging and stress. *Psychiatr Ann*. 1993;23(7):396–403.
9. Muller DJ, et al. Pharmacogenetics of tardive dyskinesia. *J Neural Transm*. 2013;120(4):649–662. doi:10.1007/s00702-012-0948-5
10. Kivell BM, et al. Epigenetic regulation in tardive dyskinesia. *Prog Neuropsychopharmacol Biol Psychiatry*. 2018;81:67–74. doi:10.1016/j.pnpbp.2017.09.001
11. Carbon M, Hsieh CH, Kane JM, Correll CU. Tardive dyskinesia prevalence in the year 2000: a meta-analysis of contemporary studies. *J Clin Psychiatry*. 2018;79(4):17r11776.
12. Carbon M, Hsieh CH, Kane JM, Correll CU. Tardive dyskinesia: prevalence, incidence, and risk factors. *J Clin Psychiatry*. 2017;78(3):e264–e278. doi:10.4088/JCP.16r10832
13. Jeste DV, Caligiuri MP. Tardive dyskinesia. *Schizophr Bull*. 1993;19(2):303–315. doi:10.1093/schbul/19.2.303
14. Warner J, D'Arcy C, Crowe M. Prevalence of tardive dyskinesia in treated schizophrenia. *Psychiatry Res*. 2013;205(1–2):93–102.
15. Zhang X, Li L, Wang X, et al. Prevalence and risk factors of tardive dyskinesia in schizophrenia: a large-scale study in China. *J Clin Psychopharmacol*. 2019;39(5):504–510. doi:10.1097/JCP.0000000000001079
16. Caroff SN, Hurford I, Lybrand J, Campbell EC. Movement disorders induced by antipsychotic drugs: implications of the CATIE schizophrenia trial. *Neurol Clin*. 2011;29(1):127–148. doi:10.1016/j.ncl.2010.10.002
17. Mentzel TQ, van der Molen M, Boot AB, et al. The impact of stigma on treatment outcomes in tardive dyskinesia. *Soc Psychiatry Psychiatr Epidemiol*. 2016;51(3):527–533.
18. McGlashan TH, Johannessen JO. Early detection and intervention with schizophrenia: rationale. *Schizophr Bull*. 2006;32(3):792–796.
19. Suresh K, Chandrashekara S. Sample size estimation and power analysis for clinical research studies. *J Hum Reprod Sci*. 2012;5(1):7–13. doi:10.4103/0974-1208.97779
20. Schooler NR, Kane JM. Research diagnoses for tardive dyskinesia. *Arch Gen Psychiatry*. 1982;39(4):486–487. doi:10.1001/archpsyc.1982.04290040080014
21. Kane JM, Correll CU, Nierenberg AA, et al. The Abnormal Involuntary Movement Scale (AIMS) and its utility in monitoring tardive dyskinesia in clinical trials. *J Clin Psychopharmacol*. 2018;38(7):707–715.
22. Nasrallah HA, Morosini P, Gagnon DD. Reliability, validity, and ability to detect change of the personal and social performance scale in patients with stable schizophrenia. *Psychiatry Res*. 2007;161(2):213–224. doi:10.1016/j.psychres.2007.11.012
23. Tenback DE, van Harten PN, van Os J. Non-therapeutic risk factors for onset of tardive dyskinesia in schizophrenia: a meta-analysis. *Schizophr Res*. 2017;191:117–124.
24. Jeste DV, Lacro JP, Bailey A, Rockwell E, Harris MJ, Caligiuri MP. Age-related modifications of risk factors for tardive dyskinesia. *Arch Gen Psychiatry*. 1999;56(4):356–362. doi:10.1001/archpsyc.56.4.356
25. Bhatia KP, Marsden CD. The behavioral and motor consequences of focal lesions of the basal ganglia in man. *Brain*. 2004;127(3):592–609.
26. Yassa R, Jeste DV. Gender differences in tardive dyskinesia: a critical review of the literature. *Schizophr Bull*. 1992;18(4):701–715. doi:10.1093/schbul/18.4.701