A Study on Drug-Induced Tardive Dyskinesia: Orofacial Musculature Involvement and Patient’s Awareness

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Abstract

Objective: Schizophrenia is a psychiatric disorder that requires long-term treatment. Long-term antipsychotic treatment is often associated with the emergence of tardive dyskinesia (TD), the severity of which is measured by Abnormal Involuntary Movement Scale (AIMS). This study examined the relationship among TD, orofacial musculature activity, and patient’s awareness of AIM. The knowledge would help dentists to deliver oral care for schizophrenics with TD.

Materials and Methods: We identified 317 patients from a standard, data sharing initiative, of whom 38.3% exhibited AIMS score of 2 to 15. The patient demographics, drug history, details of AIMS were subjected to descriptive and inferential statistical analysis using SPSS with P≤0.05 as significance.

Results: The mean of only orofacial features (n = 56) was 3.43 ± 2.68. Muscles of facial expression was involved in nine (7.9% of all TD), lip/perioral area in 27 (23.68%), jaw in 52 (45.61%), and tongue in 77 (67.54%). The patient’s perception of AIM precipitated stress when involving jaw, tongue, limbs, and trunk was statistically significant (P≤0.05). The multiple regression model statistically significantly predicted TD for factors considered.

Conclusion: Around 1% of global population is being diagnosed with schizophrenia, carry an inherent risk of developing TD. They might have orodental care requirements, including
prosthodontic and restorative services. Primary physicians and dentists need to be aware of TD and its mechanism for appropriate patient management.

**Keywords**

Antipsychotics, movement disorders, oral abnormal movements, oral health care, schizophrenia, tardive dyskinesia

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**Introduction**

Oral health and mental health are integral parts of general health. There has been recent call for considering a multidisciplinary, multiorgan inclusive consideration for proper oral health. [1] The mental disorders and consequent drug therapies carry an inherent risk for orofacial-dental disorders. [2] One of these side effects is least studied in literature is tardive dyskinesia (TD). It is a nongoal-related, repetitive, involuntary movement disorder that is often attributed to prolonged neuroleptic and other similar drug intake. It was first described as an entity in 1959 by Sigwald with cephalic involvement, which they referred as “facio-bucco-linguo-masticatory dyskinesia,” later renamed as “bucco-linguo-masticatory (BLM) syndrome” and modified as “tardive dyskinesia” by Uhrbrand and Faurbye in 1960. [3–7] By definition, TD is initiated and progresses after administration (usually long-term, but reported with short term) of neuroleptic such as phenothiazines, butyrophenones, and thioxanthenes. [4] These drugs may interfere with dopamine transmission in the brain.

The exact mechanism of TD has not been elucidated. There are several hypothesis proposed. It includes D2 receptor upregulation with subsequent hypersensitivity, GABA insufficiency, increased opioids (encephalin and dynorphin), glutamate and excitotoxicity, oxidative stress and cell injury, and genetic susceptibility. It has also been shown that typical antipsychotics tightly bind and would remain attached to D2 receptors for a longer time (a few days) than newer “atypical” agents (12–24 h). Thus, typical antipsychotics produces the more antipsychotic effect as well as higher tendency to produce TD. [8–17] In a large-scale meta-analysis involving 34,555 patients in between 1959 and 1979 showed the prevalence of TD between 20% and 50% of all patients on neuroleptics. [18] Recent analysis of studies published during 2000 to 2015 involving 11,493 patients identified, a global TD prevalence of 25.3% among antipsychotic drugs users. [9,17,19–21]

A most common manifestation of TD is orofacial chorea, akin to the spontaneous variety and involves 80% of TD. The cranio cervical region, often the “BLM triad” is most commonly involved. It includes repetitive and stereotypic oral movements including but not limiting to facial grimacing, tongue protrusion, puckering, smacking/licking of lips, side-to-side jaw motion, involuntary jaw opening, twisting, curling or protrusion of the tongue, chewing or lateral jaw movements, pursing, sucking, pouting, or puckering of the lips, facial tics, frequent eye blinking, and even dysphagia. Most of the oral TD does not cause a de novo pain or disabilities but can pose severe sociological impairment/isolation, distress, embarrassment, anxiety, depression, and even stigmatization. The movements may precipitate oral problems, including oral ulceration, speech impairment, decreased salivation (due to other side effects of the drugs), and may aggravate issues especially with dentures.
and implant placement\cite{4-6,15,16}. As the oral/perioral region are commonly involved, the patient may present to dentists for management as well as dentist may face problem while rehabilitating TD patients. In addition, as the movements in oral tissues can be well-observed, deep knowledge of etiopathogenesis and TD presentation in oral region, could help the psychiatrist for early diagnosis and management of TD.

Reports of TD are less common in neurological and psychiatric literature, and there is a paucity of reports on TD in general literature, especially the extent of oral manifestation and awareness patterns\cite{4,5}. The present manuscript aims to describe in detail the orofacial characteristics of TD with a stress on self-awareness.

Materials and Methods

As reported earlier, the prospective and retrospective methods used to study TD have inherent issues\cite{12,22}. Data used in this manuscript were obtained from the SchizConnect database (http://schizconnect.org), Collaborative Informatics and Neuroimaging Suite Data Exchange tool (http://coins.mrn.org/dx), and Mind Research Network\cite{23,24}. The investigators within SchizConnect or those who contributed to the design and implementation of SchizConnect and/or provided data but did not participate in analysis or writing of this report. All data were downloaded as .CSV format, entered, and analyzed using Statistical Package for Social Services (SPSS, Version 23; IBM, Armonk, New York, USA). Descriptive statistics and inferential statistics were performed as outlined below. $P \leq 0.05$ was taken as significant.

Baseline data of patients in SchizConnect database, who had the Abnormal Involuntary Movement Scale (AIMS)\cite{25,26} recorded, were only included in this study. AIMS is a universally accepted, validated questionnaire that documents the AIM on a 5-point questionnaire with 12 questions. It contains four questions on orofacial movements, three on extremities-trunk movements, three on global judgment, and last two relates to dental status. Only data of those with demographic details of gender, AIM score, and disease status were considered for this study.

As we intended to study the influence of TD on dental status, we employed only the first 10 questions, eliminating the dental status to arrive at the AIM score ($\geq 2$). From this, the AIM score, TD (presence/absence), orofacial AIM, and limb-trunk AIM scores were computed. Details of the disease, age, gender, the auto-calculated sum of all olanzapine equivalent doses taken by the participant, the auto-calculated sum of all chlorpromazine equivalent doses taken by the patient were acquired. The features were compared against the perception of patient’s awareness of AIM. The TD status was compared with demographic parameters and AIMS. The subscales of orofacial and limb-trunk AIM scores was then used to classify the patients to have orofacial AIM, limb-trunk AIM, both together or no AIM. The parameters were compared using appropriate statistics. To identify the relationship, AIMS parameters was assessed for correlation with TD, AIM (muscles of facial expression, lips and perioral area, jaw, tongue), severity of AIM, incapacitation due to AIM, patient’s awareness of AIM, AIM score, and TD. To identify the most important factor that contributes to AIM score, regression test was performed.
Result

The search yielded 317 patients from two studies, of whom most of the relevant data were available for 298 patients. The study group were on antipsychotic medications for schizophrenia (Strict, n = 161), (Broad, n = 89), schizoaffective (n = 38), and bipolar disorder (n = 10). The AIM score was 0 in 160 (53.5%) and 1 in 24 (8.11%) patients. The rest 38.3% had a score ranging from 2 to 15 with a mean of 5.82± 3.56 and a median of 5. Only 114 (38.3%) had TD. The mean range of only orofacial features (for four parameters, n = 56) was 3.43 ±2.68 (1–12), only limb-trunk features (three parameter, n = 21) was 3.48 ±2.91 (1–11), whereas for combined (n = 57), it was 7.33 ±3.69 (2–15). Muscles of facial expression was involved in nine (7.9% of all TD), lip/perioral area in 27 (23.68%), jaw in 52 (45.61%), and tongue in 77 (67.54%).

Table 1 shows the difference between demographic, clinical features and drug characteristics between TD and non-TD. Denture wearing and sum of equivalent olanzapine and chlorpromazine were not significant, whereas others were statistically significant. The patient’s perception of AIM precipitated stress when involving jaw, tongue, limbs, and trunk was statistically significant, whereas sex, disease, muscles of facial expression, and lip/perioral area movements were not significant [Table 2].

The data indicated that patients have been either on a mono/ multidrug therapy and drugs were often changed in visits. As this part of the data was obscure, the type of drugs, duration, and frequency were not included for this study. The sum of total equivalent doses of chlorpromazine and olanzapine was not statistically significant between grades of TD in all demographic parameters and contributing factors, except for olanzapine in lip/perioral musculature, were it was significant (P = 0.029).

It was observed that the non-TD group had relatively young age as compared to TD group, when all parameters were compared [Tables 1 and 3]. Correlation of AIM score, TD, and various oral abnormal movements was performed using correlation statistics. The muscles did not correlate much with each other, whereas other parameters were correlated significantly [Table 4].

Table 5 shows the difference among only orofacial AIM, only limb/trunk AIM, combined AIM in terms of other parameters. Among non-TD (n = 184), 12 (6.52%) cases had only orofacial movements, and eight (4.35%) cases had limb movements. In TD, there was exclusive orofacial (n = 44, 38.6%), limb-trunk (n = 13, 11.4%), and combined (n = 57, 50%) pattern. All parameters exhibit a distinct pattern between the four subcategories. However, denture wearing was not statistically significant [Table 5].

Logistic regression test were performed with clinical parameters for AIM scores. There was linearity as assessed by partial regression plots and a plot of studentized residuals against the predicted values. There was independence of residuals, as assessed by a Durbin-Watson statistic of 1.958. There was homoscedasticity, as assessed by visual inspection of a plot of studentized residuals versus unstandardized predicted values. There was no evidence of multicollinearity, as assessed by tolerance values greater than 0.1. There were no studentized deleted residuals ≥±3 standard deviations, no leverage values ≥0.2, and values for Cook’s

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distance > 1. The assumption of normality was met, as assessed by a $Q-Q$ plot. The multiple regression model statistically significantly predicted survival, $R(14, 283) = 248.77$, $P < 0.0005$, adjusted $R^2 = 0.93$. All variables added statistically significantly to the prediction, $P \leq 0.05$. Regression coefficients and standard errors can be found in Table 6.

**Discussion**

Drugs for psychiatric disorders causes a specific pattern of orodental diseases. Uncoordinated muscle movement disorders are a part of this spectrum and has been increasingly reported.\[4–6\] In normal individuals, movements are planned at the prefrontal cortex and the information passed on to the premotor cortex, supplementary motor area, and then to the primary motor cortex. The upper motor neurons which control the facial and oral movements are situated near the Sylvian fissure and axons converge and descend in the cerebral peduncle to the midbrain forming corticobulbar tract or spinal cord corticospinal tract. The neurons synapse with motor nuclei of cranial nerves to serve the orofacial musculatures. The extrapyramidal network system (EPS) is a network of neural fibers associated with coordination of movement and forms a part of the motor system. The EPS arise from pons, medulla, and are modulated by various part of CNS, including striatum and basal ganglia (BG) with dopamine being the main neurotransmitter. The function of EPS includes control of muscle tone, body posture, harmonize motor activity, and modulate functions such as the finer aspects of voluntary and involuntary movements.\[6\]

The BG regulates the initiation, grading, and control of the amplitude and direction of movement. It modulates to create fine and coordinated movements. When there is biochemical or structural abnormalities in this modulation mechanism, the BG loses its control causing unwanted motor activity.\[6,12,27\]

Movements are also modulated in the EPS via a “direct” or “indirect” pathway. The direct pathway projects from motor striatum to globus pallidus interna (GPI) and facilitates “go” signal. The indirect pathway projects in to the GPI via globus pallidus externa and subthalamic nucleus to mediate “stop” signals. Dopamine at D1 receptors in direct pathway interact with NMDA receptors, whereas the D2 receptors in indirect pathway inhibit “stop” signals, thereby causing “more go.”\[12\]

In schizophrenic brain, there appears to be too much of dopamine release. The chronic D2 receptor blockade via the antipsychotic drugs, in the motor striatum causing upregulation of supersensitive D2 receptors, often in motor striatum, causing “more go” signals, causing abnormal, hyperkinetic movements. In addition, different parts of the brain react differentially to chronic D2 blockade contributing mixed or variation in signals.\[12\] The mechanism of TD is not completely elucidated, and there has been no plausible explanation why orofacial musculature, particularly tongue is more commonly affected than other parts of the body.

The orofacial component has been described as the most common sign of TD. There is a paucity of general literature with respect to the extent of the orofacial musculature involvement, self-perception, awareness, and differences in detail between non-TD and TD.

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This manuscript aimed to address the lacunae so as to design prospective studies to understand the mechanism of TD development. In this complete random sample of patients on antipsychotics, the TD prevalence of 38.26% was observed. Twenty more cases had milder symptoms that could not be called as TD as per definition. Among non-TD (n = 184), 12 (6.52%) cases had only orofacial movements, and eight (4.35%) cases had limb movements. In TD, there was exclusive orofacial (n = 44, 38.6%), limb-trunk (n = 13, 11.4%), and combined (n = 57, 50%) pattern. In all, 113 patients (37.92%) had at least one feature suggestive of orofacial TD, whereas only 78 patients (26.17%) had features of limb-trunk TD. This trend clearly indicates that orofacial AIM occurs most commonly in TD. Among orofacial musculatures, tongue is the most commonly involved site, particularly even when positioned at rest. Instruments to measure the tongue forces in TD have been built to identify even early TD so as to initiate treatment.[28,29] This trend has been previously reported by TD reports from China.[17] Identification of the offending drug and concentration is vital for management of orofacial TD. Removal of the offending drug is the primary approach, whereas motor suppressive medications may be another therapeutic options that needs to be undertaken with caution.[4] Dental treatment of TD patients is challenging. Protection to tongue and other vital oral structures is to be taken before commencing treatment. Every care needs to be taken to ensure that instruments do not harm the TD patients.

The TD and non-TD presentations differ distinctly with age. The non-TD has a distinctly lower age than the TD group. This was consistent with previous reports.[10,13,18,19] In addition, the drug dose/total dose-equivalents of drugs were also significant across the TD/ non-TD groups. This indicates that the duration of the use of drug could be a major factor that determines the TD outcome. The difference in age is in support of this fact. As the data availability for length of drug use was limited, no valuable information could be further elicited. In the regression model, the adjusted $R^2$ of 0.93 indicates that the model could explain only up to 93% of the factors considered. The other factors such as type of antipsychotics (typical/atypical), duration of use, or frequency of use may contribute to the remaining 7%. Further studies have to confirm the role of these factors. These results are in line with the previous reports of TD from Chinese patients.[17]

There is a difference in correlation pattern between AIM score to that of orofacial musculatures. With respect to the muscles of mastication, AIM was only related significantly to lips/perioral musculature, whereas the lips/perioral musculature related significantly to all orofacial muscles. Jaw and tongue musculature AIM were not statistically significant with muscles of mastication TD. Patient’s awareness of AIM did not correlate significantly with muscles of mastication AIM. This indicates that the different parts of the orofacial musculatures react differently to the TD pathogenesis. Tongue appears to be the frequently involved orofacial musculature, whereas muscles of facial expression the least. Involvement of tongue poses additional issues such as frequent trauma to tongue, stability issues posed, whereas treating with removable dentures and even may pose a significant problem while treating them.[30] There has been several case reports in this regard and even an attempt to diagnose early TD with help of the tongue force.[4–7,29,30]
Among the orofacial musculature involvement, the jaw and tongue movements only caused varying level of distress, but this did not carry any statistical significant difference in the muscles of facial expression and lip/perioral musculature AIM. The regression statistics reveal that a significant number of patients with AIM score (≥2) have denture or tooth-related issues with a standardized coefficients $\beta = 0.037$ and unstandardized coefficient $\beta = -0.397$, $P = 0.044$. This indicates that a significant number of the study population with AIM have orodental problems. This subset of patients needs dentist attention, and this fact also underlines the need for the dentist, to understand more about TD in detail. In addition, it has been shown that the cognition deficits is relatively higher among those schizophrenics that are affected by orofacial TD.[3,31]

**Study limitations**

The study has inherent methodological limitations of the secondary data analysis of TD.[12] Cutoff values of AIM score are often varied which can lead to varied independent conclusions.[17,25,26] The frequency of movement, muscle tone/feedback, and so on have not be accounted in the database, in future should be considered. Intra and interobserver variability of scoring, reliability of AIM scores are also some factors that need to be taken in consideration. Studies with large samples and followed longitudinally needs to be undertaken to verify the findings of the present study.

**Clinical translation**

Quality of life in schizophrenic patients are varied, depending on the progression of the condition and often linked to their disease status and medications.[32] The medication side effects are measured by various scales, and AIMS is a widely used scale for measuring movement disorder.[26] With oral involvement being much early and common in TD, an alert and informed psychiatrist would diagnose/manage TD better. Hence, there is a need for the present study.

About 1% of global population are being diagnosed with schizophrenia and are treated, often with typical and atypical antipsychotics.[33] With the longevity of life increasing, the number of patients on these drugs living with increased life span are bound to increase. In addition, with prolonged use of drugs, especially atypical first-generation neuroleptics for economic reasons, occurrence of TD is bound to increase. Increased geriatric population with/without psychiatric drug prescription may present to dentists or primary care physicians for treatment. They would need more knowledge to provide medical guidance to TD patients. Examination of orofacial aspects of TD would yield valuable clues about the initiation of extrapyramidal syndrome in these patients that would help to identify, monitor, intervene, or successfully manage the condition, increasing the quality of life in these patients.

**Conclusion**

TD is a common, understudied side effect of first-generation neuroleptics, which are commonly prescribed in developing and underdeveloping countries. Tongue is the major orofacial muscle to be involved in TD, which the patient perceives and is stressed due to this
disorder. Duration of drug use and age was crucial factors that determine TD, whereas dose of drug/ drug equivalence is not. TD patients often have dental issues, and most of them are in need of dental treatments. Knowledge of orofacial TD are important for primary care physicians and psychiatrist to identify the initial manifestation to understand, identify, and treat the same at presentation of early signs and symptoms.

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Table 1:

Characteristics of the study population based on tardive dyskinesia and nontardive dyskinesia

|                          | Non-TD                     | TD                     | P value |
|--------------------------|----------------------------|------------------------|---------|
| Age                      | In years 34.64 ± 11.60     | 42.35 ± 14.16          | 0.000   |
| Age of initial diagnosis | In years 22.07 ± 8.3       | 23.61 ± 9.58           | 0.238   |
| Sex                      | Male 143 (77.7)            | 92 (80.7)              | 0.54    |
|                          | Female 41 (22.3)           | 22 (19.3)              |         |
| Disease                  | Bipolar disorder 7 (3.8)  | 3 (2.6)                | 0.061   |
|                          | Schizoaffective 30 (16.3)  | 8 (7)                  |         |
|                          | Broad schizophrenia 48 (26.1)| 41 (38)               |         |
|                          | Strict schizophrenia 99 (61.5)| 62 (38.5)             |         |
| First degree relative with psychiatric illness | No 88 (83.8) | 69 (83.1) | 0.527 |
|                          | Yes 17 (16.2)             | 14 (16.9)              |         |
| Positive and negative symptom scale | Positive scale 15.11 ±4.55 | 16.38 ±5.03 | 0.089 |
|                          | Negative scale 14.96 ±5.52 | 15.96±5.92            | 0.262   |
| General psychology scale | 28.93 ± 10.35             | 29.8 ±8.63             | 0.561   |
| Overall scale            | 58.87 ± 17.79             | 61.9±15.12             | 0.249   |
| Muscles of facial expression | Mild 0 | 7 (2.3) | 0.003 |
|                          | Minimal 3 (1.6)           | 2 (1.8)                |         |
|                          | None 181 (98.4)           | 105 (92.1)             |         |
| Lip and perioral area    | Mild 0                    | 7 (6.1)                | 0.000   |
|                          | Minimal 0                 | 16 (14)                |         |
|                          | Moderate 4 (3.5)          | 3 (2.6)                |         |
|                          | None 184 (100)            | 87 (76.3)              |         |
| Jaw                      | Mild 0                    | 24 (21.1)              | 0.0000  |
|                          | Minimal 3 (1.6)           | 25 (21.9)              |         |
|                          | Moderate 3 (2.6)          | 0                      |         |
|                          | None 181 (98.4)           | 62 (54.4)              |         |
| Tongue                   | Mild 0                    | 30 (26.3)              | 0.0000  |
|                          | Minimal 6 (3.3)           | 44 (38.6)              |         |
|                          | Moderate 0                | 2 (1.8)                |         |
| Severity           | Incapacitation | Neck, shoulder, hip | Lower limbs | Upper limbs |
|--------------------|----------------|---------------------|-------------|-------------|
| None               | 0              | 0                   | 0           | 0           |
| Mild               | 0              | 0                   | 1 (0.5)     | 0           |
| Moderate           | None           | 1 (0.5)             | 3 (2.6)     | 7 (3.8)     |
| Severe             | None           | 0                   | 0           | 0           |
| Minimal            | None           | 1 (0.5)             | 1 (0.5)     | 0           |
| Moderate           | Minimal        | 0                   | 0           | 0           |
| Severe             | None           | 0                   | 0           | 0           |
| Minimal            | None           | 0                   | 0           | 0           |
| Moderate           | None           | 0                   | 0           | 0           |

| P value            |                |                     |             |             |
|--------------------|----------------|---------------------|-------------|-------------|
| Non-TD             | 0.0000         | 0.021               | 0.000       | 0.000       |

| Awareness          | Current problem with teeth/dentures | Denture wearing | Are dentures usually worn | |
|--------------------|-------------------------------------|-----------------|---------------------------|---|
| No                 | 180 (97.8)                          | 10 (8.8)        | 2 (1.5)                   | No |
| Yes                | 173 (98)                            | 11 (6)          | 102 (89.5)                | Yes|
| No                 | 184 (100)                           | 91 (79.8)       | 6 (5.3)                   | No |
| Yes                | 174 (94.6)                          | 107 (79.9)      | 12 (10.5)                 | No |

| P value            |                |                     |             |             |
|--------------------|----------------|---------------------|-------------|-------------|
| Non-TD             | 0.0000         | 0.000               | 0.000       | 0.000       |
| Study Parameter                                      | Non-TD            | TD             | P value |
|-----------------------------------------------------|-------------------|----------------|---------|
| Yes                                                 | 10 (5.4)          | 7 (6.1)        |         |
| The autocalculated sum of all olanzapine equivalent doses taken by the participant | 398.48 ±918.21    | 352.34±371.74  | 0.923   |
| The autocalculated sum of all CPZ equivalent doses taken by the participant | 480.04 ±956.9     | 429.8 ± 397.45 | 0.609   |
| Duration of treatment at outpatient setting (months)| 81.75 ± 89.52     | 144.47 ± 149.93| 0.015   |
| Duration, living with treatment (in years)          | 11.85 ± 11.22     | 19.57±13.38    | 0.000   |

* ± Indicates standard deviation; value inside brackets “( ),” expressed as percentages (%).
Table 2:
Characteristics of study population based on awareness of abnormal involuntary movements

| Aware, with distress | No awareness | P value |
|---------------------|--------------|---------|
| **Mild** | **Moderate** | **Nil** |
| Age of patient (in years) | 51.44 ± 8.34 | 66 | 40.86 ± 15.01 | 36.5 ± 12.59 | 0.000 |
| Treatment duration in OP (months) | 160.5 ± 150.97 | 60 | 158.46 ± 174.65 | 96.83 ± 107.06 | 0.829 |
| Living with disorder for (years) | 33 ± 10.96 | 39 | 19.21 ± 13.98 | 13.41 ± 11.64 | 0.028 |
| Age at initial diagnosis (years) | 19.67 ± 5 | 23 ± 5.66 | 23.36 ± 9.61 | 22.82 ± 8.99 | 0.226 |
| PANSS | | | | | |
| Positive | 16.38 ± 3.66 | 10 | 16.21 ± 4.36 | 15.58 ± 4.94 | 0.592 |
| Negative | 19.5 ± 5.63 | 13 | 13.44 ± 3.38 | 15.54 ± 5.94 | 0.06 |
| GPS | 31.5 ± 4.69 | 22 | 29.5 ± 7.99 | 29.2 ± 10.13 | 0.798 |
| Overall | 67.38 ± 6 | 45 | 58.71 ± 11.87 | 60.19 ± 17.78 | 0.477 |
| Sex | | | | | |
| Male | 8 (3.2) | 0 | 29 (12.3) | 198 (84.3) | 0.056 |
| Female | 2 (3.2) | 2 (3.2) | 7 (11.1) | 52 (82.5) | |
| Disease | | | | | |
| Bipolar disorder | 0 | 0 | 3 (30) | 7 (70) | 0.118 |
| Schizoaffective | 1 (2.6) | 1 (2.6) | 2 (5.3) | 34 (89.5) | |
| Broad schizophrenia | 4 (4.5) | 0 | 17 (19.1) | 68 (76.4) | |
| Strict schizophrenia | 5 (3.1) | 1 (0.6) | 14 (8.7) | 141 (87.6) | |
| Muscles of facial expression | | | | | |
| Mild | 0 | 0 | 0 | 7 (100) | 0.406 |
| Minimal | 1 (20) | 0 | 1 (20) | 3 (60) | |
| None | 9 (3.1) | 2 (0.7) | 35 (12.2) | 240 (83.9) | |
| Lip and perioral area | | | | | |
| Mild | 1 (14.3) | 0 | 2 (28.6) | 4 (57.1) | 0.259 |
| Minimal | 2 (12.5) | 0 | 3 (18.8) | 11 (68.8) | |
| Moderate | 0 | 0 | 0 | 4 (100) | |
| None | 7 (2.6) | 2 (0.7) | 31 (11.4) | 231 (85.2) | |
| Jaw | | | | | |
| Mild | 4 (16.7) | 2 (8.3) | 10 (41.7) | 8 (33.3) | 0.000 |
| Minimal | 1 (3.6) | 0 | 8 (28.6) | 19 (67.9) | |
| Moderate | 0 | 0 | 1 (33.3) | 2 (66.7) | |
| None | 5 (2.1) | 0 | 17 (7) | 221 (90.9) | |
| Tongue | | | | | |
| Mild | 5 (16.7) | 0 | 14 (46.7) | 11 (36.7) | 0.0000 |
| Minimal | 1 (2) | 0 | 9 (18) | 40 (80) | |
|                     | Aware, with distress |       |       |       |       |
|---------------------|----------------------|-------|-------|-------|-------|
|                     | Mild | Moderate | Nil |       |       |
|         |       |         |     |       |       |
| Moderate | 0    | 0       | 0   | 2 (100) |       |
| None    | 4 (1.9) | 2 (0.9) | 13 (6) | 196 (91.2) |       |
| Severe  | 0    | 0       | 0   | 1 (100) |       |
| Upper limbs |       |         |     |       |       |
| Mild    | 6 (19.4) | 0       | 14 (45.2) | 11 (35.5) | 0.0000 |
| Minimal | 1 (2.8) | 0       | 7 (19.4) | 28 (77.8) |       |
| Moderate | 0    | 0       | 1 (33.3) | 2 (66.7) |       |
| None    | 3 (1.3) | 2 (0.9) | 14 (46.1) | 209 (91.7) |       |
| Lower limb |       |         |     |       |       |
| Mild    | 3 (16.7) | 0       | 8 (44.4) | 7 (38.9) | 0.0000 |
| Minimal | 0    | 0       | 7 (36.8) | 12 (63.2) |       |
| None    | 7 (2.7) | 2 (0.8) | 21 (8) | 231 (88.5) |       |
| Neck, shoulder, hip |       |         |     |       |       |
| Mild    | 0    | 0       | 0   | 2 (100) | 0.004 |
| Minimal | 0    | 0       | 1 (50) | 1 (50) |       |
| None    | 2 (40) | 0       | 0   | 3 (60) |       |
| Severity |       |         |     |       |       |
| Mild    | 9 (21.4) | 2 (4.8) | 17 (40.5) | 14 (33.3) | 0.0000 |
| Minimal | 1 (2) | 0       | 11 (22) | 38 (76) |       |
| Moderate | 0    | 0       | 0   | 5 (100) |       |
| None    | 0    | 0       | 8 (4) | 193 (96) |       |
| Incapacitation |       |         |     |       |       |
| Mild    | 2 (40) | 0       | 1 (20) | 2 (40) |       |
| Minimal | 3 (27.3) | 0       | 4 (36.4) | 4 (36.4) |       |
| Moderate | 1 (16.7) | 0       | 0   | 5 (83.3) |       |
| None    | 4 (1.5) | 2 (0.7) | 30 (10.9) | 239 (86.9) |       |

* ± Indicates standard deviation; value inside brackets “(),” expressed as percentages (%).
Table 3:
Comparison of mean age (in years ± standard deviation) between tardive dyskinesia patients and nontardive dyskinesia patients based on parameters considered

| Parameter                      | Non-TD                  | TD          |
|--------------------------------|-------------------------|-------------|
| **Muscles of facial expression** |                         |             |
| Mild                           | -                       | 47.29 ± 15.25 |
| Minimal                        | 24.33 ± 2.52            | 40.5 ± 17.68 |
| None                           | 34.81 ± 11.62           | 42.05 ± 14.13 |
| **Lip and perioral area**      |                         |             |
| Mild                           | -                       | 48.71 ± 16.09 |
| Minimal                        | -                       | 45.88 ± 14.9 |
| Moderate                       | -                       | 50 ± 5.72   |
| None                           | 34.64 ± 11.60           | 40.8 ± 13.95 |
| **Jaw**                        |                         |             |
| Mild                           | -                       | 48.74 ± 14.23 |
| Minimal                        | 37 ± 11.79              | 40.71 ± 13.98 |
| Moderate                       | -                       | 37 ± 23.64  |
| None                           | 34.6 ± 11.63            | 40.87 ± 13.40 |
| **Tongue**                     |                         |             |
| Mild                           | -                       | 45.13 ± 13.97 |
| Minimal                        | 37.67 ± 15.77           | 38.95 ± 14.59 |
| Moderate                       | -                       | 41 ± 19.8  |
| None                           | 34.53 ± 11.48           | 43.94 ± 13.49 |
| Severe                         | -                       | 50          |
| **Upper limbs**                |                         |             |
| Mild                           | -                       | 44.81 ± 12.99 |
| Minimal                        | 34.57 ± 11.312          | 42.93 ± 14.54 |
| Moderate                       | -                       | 54.67 ± 4.93 |
| None                           | 34.64 ± 11.65           | 39.69 ± 14.39 |
| **Lower limb**                 |                         |             |
| Mild                           | -                       | 31.5 ± 4.95 |
| Minimal                        | -                       | 51.4 ± 8.56 |
| None                           | 34.49 ± 11.58           | 42.12 ± 14.31 |
| **Neck, shoulder, hip**        |                         |             |
| Mild                           | -                       | 31.5 ± 4.95 |
| Minimal                        | -                       | 51.4 ± 8.56 |
| None                           | 34.49 ± 11.58           | 42.12 ± 14.31 |
| **Severity**                   |                         |             |
| Mild                           | -                       | 46.9 ± 14.15 |
| Incapacitation          | Non-TD       | TD           |
|-------------------------|--------------|--------------|
| Minimal                 | -            | 37.73 ± 12.44|
| Moderate                | -            | 46.4 ± 12.12 |
| None                    | 34.64 ± 11.60| 43.47 ± 16.27|

| Awareness               | Non-TD       | TD           |
|-------------------------|--------------|--------------|
| Incapacitation          |              |              |
| Minimal                 | -            | 47.18 ± 14.78|
| Moderate                | -            | 43.67 ± 11.93|
| None                    | 34.64 ± 11.60| 41.37 ± 14.4 |

| Awareness | Non-TD       | TD           |
|-----------|--------------|--------------|
| Incapacitation |              |              |
| Minimal   | -            | 47.18 ± 14.78|
| Moderate  | -            | 43.67 ± 11.93|
| None      | 34.64 ± 11.60| 41.37 ± 14.4 |

| Current problem with teeth/dentures | Non-TD       | TD           |
|-------------------------------------|--------------|--------------|
| No                                  | 34.78 ± 11.60| 39.81 ± 13.63|
| Yes                                 | 32.55 ± 11.96| 49.96 ± 13.15|

| Are dentures usually worn | Non-TD       | TD           |
|---------------------------|--------------|--------------|
| No                        | 34.38 ± 11.51| 41.67 ± 14.42|
| Yes                       | 41 ± 13.1    | 48.55 ± 10.00|

| Denture wearing | Non-TD       | TD           |
|-----------------|--------------|--------------|
| No              | 34.22 ± 11.49| 41.71 ± 14.19|
| Yes             | 41.8 ± 11.75 | 53.67 ± 7.69 |
Table 4:
Correlation of abnormal involuntary score, tardive dyskinesia, and oral abnormal movements

|                      | Muscles of facial expression | Lips and perioral area | Jaw | Tongue | Severity of AM overall | Incapacitation due to AM | Patient’s awareness of AM | AIMscore | TD |
|----------------------|-----------------------------|------------------------|-----|--------|------------------------|--------------------------|---------------------------|----------|----|
| **Muscles of**      |                             |                        |     |        |                        |                          |                           |          |    |
| facial expression   | Correlation Sig.            |                        |     |        |                        |                          |                           |          |    |
|                      | 1                            | 0.346 *                | 0.070 | 0.065  | 0.223 *                | 0.227 *                  | -0.020                    | -0.393 * | -0.185 * |
|                      | Correlation Sig.            | 0.226                  | 0.266 | 0.000  | 0.395 *                | 0.158 *                  | 0.000                     | 0.060 *  | -0.383 * |
| **Lips and**        | 0.000                       |                        | 0.346 * | 0.070  | 0.366 *                | 0.314 *                  | 0.381 *                   | -0.020  | -0.393 * |
| **perioral area**   | Correlation Sig.            | 0.000                  | 0.000 | 0.000  | 0.381 *                | 0.395 *                  | 0.158 *                   | 0.000 *  | 0.001    |
|                      |                             |                        | 0.314 * | 0.346 * | 1                      | 0.398 *                  | 0.571 *                   | 0.139 ** | -0.600 * |
|                      | Correlation Sig.            | 0.000                  | 0.000 | 0.000  | 0.000                   | 0.016                    | 0.000                     | 0.000    | 0.000    |
| **Jaw**             | 0.070                       | 0.366 *                | 1    | 0.398 * | 0.571 *                | 0.139 **                  | 0.424 *                   | -0.600 * | -0.547 * |
|                      | Correlation Sig.            | 0.226                  | 0.000 | 0.000  | 0.000                   | 0.016                    | 0.000                     | 0.000    | 0.000    |
| **Tongue**          | 0.065                       | 0.314 *                | 0.398 * | 1      | 0.592 *                | 0.246 *                  | 0.374 *                   | -0.668 * | -0.674 * |
|                      | Correlation Sig.            | 0.266                  | 0.000 | 0.000  | 0.000                   | 0.000                    | 0.000                     | 0.000    | 0.000    |
| **Severity of AM**  | 0.223 *                     | 0.381 *                | 0.571 * | 0.592 * | 1                      | 0.409 *                  | 0.569 *                   | -0.791 * | -0.846 * |
| **overall**         | Correlation Sig.            | 0.266                  | 0.000 | 0.000  | 0.000                   | 0.000                    | 0.000                     | 0.000    | 0.000    |
|                      |                             |                        | 0.314 * | 0.346 * | 1                      | 0.398 *                  | 0.571 *                   | 0.139 ** | -0.600 * |
| **Incapacitation**  | 0.000                       |                        | 0.346 * | 0.070  | 0.366 *                | 0.314 *                  | 0.381 *                   | -0.020  | -0.393 * |
| due to AM           | Correlation Sig.            | 0.000                  | 0.000 | 0.000  | 0.381 *                | 0.395 *                  | 0.158 *                   | 0.000 *  | 0.001    |
|                      |                             |                        | 0.314 * | 0.346 * | 1                      | 0.398 *                  | 0.571 *                   | 0.139 ** | -0.600 * |
|                      | Correlation Sig.            | 0.000                  | 0.000 | 0.000  | 0.000                   | 0.016                    | 0.000                     | 0.000    | 0.000    |
| **Patient’s**       | -0.020                      |                        | 0.158 * | 0.424 * | 0.424 *                | 0.424 *                  | 1                         | -0.598 * | -0.476 * |
| **awareness**       | Correlation Sig.            | 0.728                  | 0.006 | 0.000  | 0.374 *                | 0.569 *                  | 0.363 *                   | -0.571 * | -0.340 * |
| of AM               |                             |                        | 0.424 * | 0.381 * | 1                      | 0.398 *                  | 0.571 *                   | -0.791 * | -0.846 * |
|                      | Correlation Sig.            | 0.000                  | 0.000 | 0.000  | 0.000                   | 0.000                    | 0.000                     | 0.000    | 0.000    |
| **AIMscore**        | -0.393 *                    |                        | -0.608 * | -0.600 | -0.608 *                | -0.608 *                 | -0.668 *                  | -0.791 * | -0.571 * |
|                      | Correlation Sig.            | -0.728                 | 0.000 | 0.000  | 0.374 *                | 0.569 *                  | 0.363 *                   | -0.571 * | -0.598 * |
|                      |                             |                        | -0.608 * | -0.600 | -0.608 *                | -0.608 *                 | -0.668 *                  | -0.791 * | -0.571 * |
| **TD**              | -0.185 *                    |                        | -0.383 * | -0.547 | -0.674 *                | -0.846 *                 | -0.340 *                  | -0.476 * | 0.782 *  |
|                      | Correlation Sig.            | -0.258                 | 0.000 | 0.000  | 0.000                   | 0.000                    | 0.000                     | 0.000    | 0.000    |

* Correlation is significant at the 0.01 level (two-tailed).
** Correlation is significant at the 0.05 level (two-tailed).
Table 5:
Difference of abnormal movements based on characteristics studied in the study population**

|                      | Abnormal movements | P value |
|----------------------|--------------------|---------|
|                      | No                 | Only orofacial | Only limb/trunk | Both    |
| **Severity**         |                    |               |                 |         |
| Mild                 | 16 (28.6)          | 6 (14.3)      | 20 (47.6)       | 0.000   |
| Minimal              | 25 (44.6)          | 4 (19)        | 21 (36.8)       |         |
| Moderate             | 1 (1.8)            | 0             | 4 (7)           |         |
| None                 | 164 (100)          | 14 (25)       | 11 (5.5)        | 12 (21.1)|
| **Incapacitation**   |                    |               |                 |         |
| Mild                 | 0                  | 0             | 1 (1.8)         | 0.0000  |
| Minimal              | 0                  | 3 (14.3)      | 2 (3.5)         |         |
| Moderate             | 0                  | 2 (9.5)       | 9 (15.8)        |         |
| None                 | 164 (100)          | 55 (98.2)     | 15 (71.4)       | 41 (71.9)|
| **Awareness of distress** |                |               |                 |         |
| Aware, mild          | 0                  | 3 (5.4)       | 3 (14.3)        | 4 (7)   | 0.000   |
| Aware, moderate      | 0                  | 2 (3.6)       | 0               | 0       |         |
| Aware, nil           | 4 (2.4)            | 8 (14.3)      | 5 (23.8)        | 19 (33.3)|
| No awareness         | 160 (97.6)         | 43 (76.8)     | 13 (61.9)       | 34 (59.6)|
| **Current problem with teeth/dentures** |             |               |                 |         |
| No                   | 156 (95.1)         | 44 (78.6)     | 16 (76.2)       | 42 (73.7)| 0.000   |
| Yes                  | 8 (4.9)            | 12 (21.4)     | 5 (23.8)        | 15 (26.3)|         |
| **Are dentures usually worn** |             |               |                 |         |
| No                   | 157 (95.7)         | 53 (94.6)     | 19 (90.5)       | 50 (87.7)| 0.172   |
| Yes                  | 7 (4.3)            | 3 (5.4)       | 2 (9.5)         | 7 (12.3) |         |
| **Denture wearing**  | No                 | 156 (95.1)    | 50 (89.3)       | 20 (95.2)| 55 (96.5)| 0.338   |
| Yes                  | 8 (4.9)            | 6 (10.7)      | 1 (4.8)         | 2 (3.5)  |         |
| **Mean age**         | 34.56 ± 11.51      | 38.59 ± 14.81 | 42.05 ± 12.41   | 43.53 ± 13.85 | 0.000   |
| **Treatment duration in OP (months)** | 77.2 ± 83.33 | 101.21 ± 132.02 | 207.67 ± 127.55 | 152.76 ± 158.23 | 0.001   |
| **Living with disorder for (years)** | 11.39 ± 11.06 | 18.21 ± 14.59 | 19.47 ± 7.95   | 19.68 ± 13.69 | 0.000   |
| **Age at initial diagnosis (years)** | 22.19 ± 8.4 | 21.24 ± 7.29 | 25.87 ± 9.9 | 24.45 ± 10.75 | 0.182   |
| **Positive scale**   | 15.26 ± 4.61       | 17.30 ± 5.58  | 15.93 ± 3.58    | 15.03 ± 4.74  | 0.161   |
| **Negative scale**   | 15.35 ± 5.56       | 16.22 ± 5.66  | 11.93 ± 3.92    | 16.18 ± 6.27  | 0.073   |
| **General psychopathology scale** | 29.62 ± 31.15 | 31.15 ± 10.24 | 27 ± 5.48       | 27.97 ± 7.3   | 0.410   |
| **Overall scale**    | 60.14 ± 18.26      | 64.22 ± 18.31 | 54.87 ± 10.81   | 59.18 ± 13.07 | 0.317   |
|                                | Unstandardized coefficients | Standardized coefficients | t    | Sig.  | 95% Confidence interval for B |
|--------------------------------|-----------------------------|---------------------------|------|-------|-----------------------------|
|                                | B          | Std. error | Beta |      | Lower bound | Upper bound |
| Constant                       | 29.253     | 1.134      | 25.793 | 0.000 | 27.020       | 31.485       |
| Muscles of facial expression   | -2.361     | 0.186      | -0.218 | -12.718 | 0.000       | -2.727       | -1.996       |
| Lips and perioral area         | -0.969     | 0.109      | -0.174 | -8.919  | 0.000       | -1.183       | -0.755       |
| Jaw                            | -0.384     | 0.054      | -0.145 | -7.087  | 0.000       | -0.490       | -0.277       |
| Tongue                         | -0.590     | 0.068      | -0.181 | -8.715  | 0.000       | -0.723       | -0.457       |
| Severity of AIM overall        | -0.649     | 0.075      | -0.214 | -8.636  | 0.000       | -0.797       | -0.501       |
| Incapacitation due to AIM      | -0.663     | 0.121      | -0.111 | -5.494  | 0.000       | -0.901       | -0.425       |
| Patient's awareness of AIM     | -0.416     | 0.055      | -0.155 | -7.589  | 0.000       | -0.524       | -0.308       |
| Current problems with teeth and/or dentures | 0.386 | 0.191 | 0.037 | 2.026 | 0.044 | 0.011 | 0.761 |
| Are dentures usually worn?     | -0.397     | 0.266      | -0.027 | -1.494  | 0.136       | -0.920       | 0.126        |
| Denture wearing?               | 0.327      | 0.281      | 0.021 | 1.166  | 0.245       | -0.225       | 0.880        |
| Upper (arms, wrists, hands, fingers) | -0.413 | 0.050 | -0.172 | -8.274 | 0.000       | -0.511       | -0.315       |
| Lower (legs, knees, ankles, toes) | -0.989 | 0.126 | -0.146 | -7.840 | 0.000       | -1.237       | -0.741       |
| Neck, shoulders, hips          | -0.355     | 0.176      | -0.030 | -1.908  | 0.057       | -0.680       | 0.011        |