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Clinical features and neuropsychiatric comorbidities in pediatric patients with tic disorders: a retrospective chart review study from South Korea

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Abstract

Background: Tic disorders are childhood-onset neuropsychiatric disorders characterized by multiple motor or vocal tics with frequent comorbidities and a broad spectrum of phenotypic presentations. In this study, we aimed to investigate the clinical characteristics and comorbid neuropsychiatric conditions in pediatric patients with tic disorders.

Methods: We retrospectively reviewed the medical records of 119 pediatric patients (89 males, 30 females) who were diagnosed with tic disorders according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) at Uijeongbu St. Mary's Hospital, Republic of Korea, between January 2012 and July 2019.

Results: The mean age of tic onset was 6.9 years (range, 1–14) and the mean age at diagnosis was 8 years (range, 1–17). The mean lag between tic onset and diagnosis was 13.3 months (range, 0.25–132). The most common, first-presenting tics were eye blinking (50.4%), followed by jaw or lip movement (29.4%) and throat clearing (29.4%). Thirty-seven (31.1%) patients had at least one co-occurring neuropsychiatric disorder at the time of tic diagnosis. Subtypes of tic disorders, types of initial tics, and presence of neuropsychiatric comorbidities were not associated with tic severity. Tic severity was associated with greater functional impairment and tic noticeability ($p < 0.05$). A relatively shorter time to diagnosis was associated with tic severity (Spearman's $\rho = -0.14$, $p = 0.11$).

Conclusions: The evolving nature of tic expression and severity, high prevalence of neuropsychiatric comorbidities, and associated functional impairments emphasize the importance of comprehensive assessment during the disease course for determining and prioritizing goals of treatment.

Keywords: Tic disorders, Tourette syndrome, Diagnostic and statistical manual of mental disorders, Comorbidity

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Background

Tics are involuntary, stereotyped, nonrhythmic movements or vocalizations that are usually sudden and rapid [1, 2]. A broad spectrum of phenotypes ranging from mild to severe and involving any muscle group characterizes the disorders [3]. Tics are categorized as either motor or vocal, and simple or complex, based on their quality and degree of complexity [4]. They can appear isolated or in combination and may coexist or occur in orchestrated sequences. The average age of onset for tic disorders is 4–6 years, peaking between 10 and 12 years, and declining throughout adolescence [5–7].

The precise etiology of tic disorders remains undetermined; however, there is strong agreement that their presence is associated with both polygenic and environmental factors [8]. Although several susceptibility genes have been suggested, no definitive causative gene mutation or risk allele has been identified, due to various factors such as the phenotypic and genotypic heterogeneity, variations in polygenic burden, rare mutations, epigenetic factors, and gene-environment interactions [9]. Environmental factors such as prenatal exposure, perinatal complications, infections, altered immune regulation, and psychosocial stressors are implicated in the development of tic disorders [10].

Tic disorders are usually associated with mental, behavioral, and developmental comorbidities, with previous studies demonstrating that approximately 80–90% of individuals with tic disorders also present other concurrent neuropsychiatric symptoms [5, 11, 12]. Attention-deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) are the most commonly reported comorbidities, followed by depression [5, 13–15]. O'Hare et al. [16] noted that children with tic disorders and co-occurring neuropsychiatric comorbidities tend to have a lower global quality of life and more severe functional impairment. Considering the impact of associated psychopathology on the well-being of patients, an early diagnosis may allow prompt interventions that can improve quality of life, aid social skills, and facilitate academic achievement [17].

Tic disorders are clinically diagnosed on the basis of a detailed history and a neurological and psychiatric examination [4]. However, diagnostic difficulties can arise in certain circumstances because of the waxing and waning nature of tics and the variability of symptoms [18], which may impede initiating timely and appropriate interventions. The mean estimated interval between onset of tics and diagnosis is relatively long [19], with previous studies reporting a lag period ranging from 3 to 11.9 years [5, 20–22].

In this study, we aimed to investigate the clinical features and comorbid neuropsychiatric disorders in pediatric patients with tic disorders. In addition, we evaluated the effects of demographic and clinical

factors on the timing of tic disorder diagnosis and on clinical outcomes.

Methods

We retrospectively reviewed the medical charts of pediatric patients who were diagnosed with tic disorders according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) at Uijeongbu St. Mary's Hospital, Republic of Korea, between January 2012 and July 2019. Those who did not meet the diagnostic criteria or those who were lost to follow-up were excluded from this study.

Demographic and clinical data included gender, age of tic onset, age at diagnosis, types and duration of tic symptoms, tic severity at the initial clinical visit and at the most recent follow-up, and the presence of neuropsychiatric comorbidities. The diagnosis of neuropsychiatric comorbidities such as ADHD, OCD, depression, and anxiety were documented by a pediatric neurologist or a psychiatrist based on a psychiatric interview, according to the DSM-5 criteria. Developmental delay and intellectual disability were diagnosed based on the Bayley Scales of Infant Development, 3rd edition and Korean Wechsler Intelligence Scale for Children, 4th edition, respectively. The time to diagnosis of tic disorders was defined as the interval between the reported onset of tic symptoms and the timing of tic disorder diagnosis by a physician.

Severity of tics and tic-related impairment were assessed using the translated Korean version of the semi-structured, clinician-rated Yale Global Tic Severity Scale (YGTSS). The Korean version of YGTSS was developed and shown to be a valid and reliable rating scale in a previous study [23]. Tic severity was assessed by summing the total scores of motor and vocal tics on a scale from 0 to 5, in 5 separate dimensions: number, frequency, intensity, complexity, and interference. Total scores were categorized as follows: absence of tics (0), minimal tics (1–9), mild tics (10–19), moderate tics (20–39), and severe tics (40–50). A high tic score was defined as moderate or severe tics (20–50). Tic-related impairment and impact on the individual's self-esteem, family and peer relationships, and school or job functioning were rated separately on a 6-step ordinal scale (0–60).

All statistical analyses were performed with SPSS 21.0 for Windows (IBM Corp., Armonk, NY, USA). Fisher's exact test, Pearson's chi-square test, and Student's t-test were used to compare the clinical outcomes by baseline demographics. In addition, Spearman's rank correlation coefficient (ρ) and the Kruskal-Wallis test were used to analyze the relationship between the time to diagnosis of tic disorders and other variables. Univariate and multivariate logistic regression analyses were performed to identify potential predictor variables and to assess the

associations between the variables and tic severity. Statistical significance was defined at $p < 0.05$.

Ethical approval for this retrospective study was provided by the Institutional Review Board of Catholic Medical Center (IRB UC19RASI0149).

Results

Patient characteristics

We identified 119 pediatric patients (89 males, 30 females) who were diagnosed with tic disorders during the time frame of this study. The mean age of tic onset was 6.9 years (range, 1–14) and the mean age at the time of diagnosis of tic disorders was 8 years (range, 1–17). Of the 119 patients, ninety-two (77.3%) were diagnosed with provisional tic disorder and 19 (16%) with Tourette syndrome. The remaining 8 patients (6.7%) were diagnosed with chronic motor or vocal tic disorder.

The most common, first-presenting tics were eye blinking (50.4%), followed by jaw or lip movement (29.4%) and throat clearing (29.4%). In addition, head-turning or nodding (28.6%), eyeball rolling (26.9%), and arm movement (26.9%) were frequently observed (Table 1). Of the 119 patients, thirty-seven (31.1%) had at least one co-occurring neuropsychiatric disorder at the time of diagnosis of tic disorders. The most common comorbid neuropsychiatric condition was ADHD (10.9%), followed by anxiety disorder (7.6%), developmental delay or intellectual disability (6.7%), and epilepsy (6.7%) (Table 2). Eighty of 119 patients (67.2%) were treated with anti-tic medication: antipsychotics only ($n = 72$), antidepressants only ($n = 1$), and combined antipsychotics and antidepressants ($n = 7$). The remaining 39 patients (32.8%) received behavioral therapy.

Tic severity and associated impairment

Seventy-six (63.9%) children in the sample were reported to have mild symptoms, thirty (25.2%) had moderate symptoms, and the remaining thirteen (10.9%) had severe symptoms. A comparison of demographic and clinical characteristics of patients with mild tics and those with moderate to severe tics is shown in Table 3. No significant differences were found between patients diagnosed with mild tics compared to moderate/severe tics with regard to gender, age at symptom onset, age at diagnosis, or time between symptom onset and diagnosis. Subtypes of tic disorders, types of initial tics, and presence of neuropsychiatric comorbidities were not associated with tic severity. Based on multivariate regression analysis, gender, age at symptom onset, age at diagnosis, time between symptom onset and diagnosis, subtypes of tic disorders, types of initial tics, and presence of neuropsychiatric comorbidities, were not significantly related to tic severity (Table 4). However, patients with moderate to severe tics were significantly more likely to have tics that

Table 1 Patient characteristics

	Number of patients ($n = 119$)
Sex ratio (male:female)	89: 30
Age (years) at symptom onset, mean (range)	6.9 (1–14)
Age (years) at diagnosis, mean (range)	8 (1–17)
Time interval (months) between symptom onset and diagnosis, mean (range)	13.3 (0.25–132)
Subtypes of tic disorder	
Provisional tic disorder	92 (77.3%)
Chronic motor or vocal tic disorder	8 (6.7%)
Tourette syndrome	19 (16%)
Initial tic symptoms	
Eye blinking	60 (50.4%)
Jaw/Lip movement	35 (29.4%)
Throat clearing	35 (29.4%)
Head turning/Nodding	34 (28.6%)
Eyeball rolling	32 (26.9%)
Arm movement	32 (26.9%)
Palilalia	25 (21%)
Shoulder movement	23 (19.3%)
Grimacing	21 (17.6%)
Leg movement	19 (16%)
Sniffing	18 (15.1%)
Coughing	15 (12.6%)
Trunk movement	14 (11.8%)
Sighing	5 (4.2%)
Echolalia	4 (3.4%)
Coprolalia	3 (2.5%)
Grunting	3 (2.5%)
Whistling	2 (1.7%)
Spitting	1 (0.8%)

Table 2 Comorbid neuropsychiatric disorders

	Number of patients ($n = 119$)
Attention-deficit hyperactivity disorder	13 (10.9%)
Anxiety disorder	9 (7.6%)
Developmental delay/Intellectual disability	8 (6.7%)
Epilepsy	8 (6.7%)
Self-injurious behavior	4 (3.4%)
Enuresis	3 (2.5%)
Obsessive-compulsive disorder	1 (0.8%)
Depression	1 (0.8%)
Adjustment disorder	1 (0.8%)
Night terror	1 (0.8%)

Table 3 Comparison of demographic and clinical characteristics of patients based on tic severity

	Patients with mild tics (n = 76)	Patients with moderate to severe tics (n = 43)	P value
Gender (Male) ^a	55 (72.4%)	34 (79.1%)	0.41
Age (years) at symptom onset, mean (range) ^b	6.9 (1.2–14.5)	7.9 (1.3–14.3)	0.07
Age (years) at diagnosis, mean (range) ^b	7.9 (1.7–17.2)	9.1 (2.1–17.4)	0.08
Time interval (months) between symptom onset and diagnosis, mean (range) ^b	12.9 (0.25–96)	13.9 (0.25–132)	0.81
Subtypes of tic disorder ^a			
Provisional tic disorder	59 (77.6%)	33 (76.7%)	0.91
Chronic motor or vocal tic disorder	6 (7.9%)	2 (4.7%)	0.49
Tourette syndrome	11 (14.5%)	8 (18.6%)	0.55
Initial tic symptoms			
Motor tics ^a	38 (50%)	14 (32.6%)	0.06
Vocal tics ^c	4 (5.3%)	4 (9.3%)	0.45
Motor + vocal tics ^a	34 (44.7%)	25 (58.1%)	0.16
Presence of neuropsychiatric comorbidities ^a	21 (27.6%)	16 (37.2%)	0.27
Tics are noticeable to strangers ^a	38 (50%)	31 (72.1%)	0.01
Tics interfere with functioning ^a	24 (31.6%)	30 (69.8%)	< 0.05

^aChi-square test was used
^bIndependent t-test was used
^cFisher's exact test was used

were noticeable to strangers and that interfered with their daily functioning, compared to those with mild tics. When the patients were divided into three groups according to subtypes of tic disorders, no significant differences in gender, age at symptom onset, age at diagnosis, time between symptom onset and diagnosis, types of initial tics, and presence of neuropsychiatric comorbidities were observed between patients with different tic severities. Compared to those with mild tics, patients with provisional tic disorder and those with moderate to severe tics, were significantly

more likely to have tics that were noticeable to strangers and that interfered with their daily functioning.

Factors influencing time to diagnosis

The mean lag time from when tics were first noticed to diagnosis of tic disorders was 13.3 months (range, 0.25–132). Gender differences in lag time to diagnosis were observed, 10.0 months for females compared to 8.0 months for males ($p = 0.05$). No significant difference was found in the time to diagnosis between patients with

Table 4 Multivariate analysis of variables associated with tic severity

	Odds ratio (95% CI)	P value
Gender	0.67 (0.24–1.88)	0.45
Age at symptom onset	0.09 (0–1,059,041.33)	0.77
Age at diagnosis	11.79 (0–131,775,769.7)	0.76
Time interval between symptom onset and diagnosis	0.81 (0.21–3.16)	0.77
Subtypes of tic disorder		
Provisional tic disorder	1	0.37
Chronic motor or vocal tic disorder	1.43 (0.39–5.21)	0.58
Tourette syndrome	0.38 (0.04–3.37)	0.39
Initial tic symptoms		
Motor tics	1	0.77
Vocal tics	1.47 (0.26–8.13)	0.65
Motor + vocal tics	1.42 (0.50–3.97)	0.50
Presence of neuropsychiatric comorbidities	1.43 (0.58–3.52)	0.43

the presence of neuropsychiatric comorbidities, and those without ($p = 0.91$). In addition, age at symptom onset was not correlated with the time to diagnosis (Spearman's $\rho = -0.14$, $p = 0.11$). The mean time to diagnosis was shorter in patients whose initial tics were motor tics only, compared to those with vocal tics only and combined motor and vocal tics, with a mean of 5.6 months (range, 0.25–24), 21.3 months (range, 0.25–96), and 18.9 months (range, 0.25–132), respectively ($p < 0.05$). Tic severity was negatively correlated with diagnostic lag time (Spearman's $\rho = -0.18$, $p < 0.05$), that is, the more severe the tics, the less time that elapsed before a diagnosis.

Predictors of follow-up outcomes

The patients were followed up for an average of 20.2 months (range, 0.1–88.5) after the diagnosis of tic disorders. Of 119 patients, ninety-nine (83.2%) reported a greater than 50% reduction in tic severity, and twenty (16.8%) reported no changes in the tic symptoms at follow-up. To determine the factors related to favorable outcomes, we compared the characteristics of patients who achieved more than 50% reduction in symptoms with those who had no change in tic severity. Gender, age of onset, age at diagnosis, time interval between onset and diagnosis, subtypes of tic disorders, initial symptoms, tic severity at diagnosis, presence of neuropsychiatric

comorbidities, and treatment utilization did not influence likelihood of favorable outcomes (Table 5). Based on multivariate regression analysis, gender, age of onset, age at diagnosis, time interval between onset and diagnosis, subtypes of tic disorders, initial symptoms, tic severity at diagnosis, presence of neuropsychiatric comorbidities, and treatment utilization, were not significantly related to clinical outcomes (Table 6). When the patients were divided into three groups according to subtypes of tic disorders, no significant differences regarding gender, age of onset, age at diagnosis, time interval between onset and diagnosis, initial tic symptoms, tic severity at diagnosis, presence of neuropsychiatric comorbidities, or treatment utilization were observed between patients who showed different outcomes.

Discussion

Isolated and transient tics are fairly common in childhood, ranging from 11 to 20% in different studies [24–26]. Diagnostic issues may arise in certain circumstances due to the waxing and waning nature and heterogeneity of tic symptom presentation [18]. Additionally, only a few studies have evaluated how many children with transient tics would become cases of Tourette syndrome or chronic tic disorder over time [27]. Therefore, in this study we tried to delineate the clinical features of tic disorders and

Table 5 Comparison of demographic and clinical features based on clinical outcomes

	Patients with > 50% reduction in tics (n = 99)	Patients with no changes in tics (n = 20)	P value
Gender (Male) ^a	74 (74.7%)	15 (75%)	0.98
Age (years) at symptom onset, mean (range) ^b	7.1 (1.2–13.9)	8.2 (1.7–14.5)	0.12
Age (years) at diagnosis, mean (range) ^b	8.2 (1.7–17.4)	9.1 (2.4–14.9)	0.26
Time interval (months) between symptom onset and diagnosis, mean (range) ^b	13.7 (0.25–132)	11.2 (0.25–60)	0.63
Subtypes of tic disorder ^a			
Provisional tic disorder	77 (77.8%)	15 (75%)	0.78
Chronic motor or vocal tic disorder	7 (7.1%)	1 (5%)	0.73
Tourette syndrome	15 (15.1%)	4 (20%)	0.58
Initial tic symptoms ^a			
Motor tics	44 (44.4%)	8 (40%)	0.71
Vocal tics	8 (8.1%)	0	0.18
Motor + vocal tics	47 (47.5%)	12 (60%)	0.30
YGTS at diagnosis, mean (range) ^b	12.6 (0–50)	15 (0–30)	0.37
Presence of neuropsychiatric comorbidities ^a	32 (32.3%)	5 (25%)	0.51
Treatment utilization ^a			
Medication	66 (66.7%)	14 (70%)	0.77
Nonmedical treatment	33 (33.3%)	6 (30%)	0.77

YGTS Yale Global Tic Severity Scale

^aChi-square test was used

^bIndependent t-test was used

Table 6 Multivariate analysis of variables associated with clinical outcomes

	Odds ratio (95% CI)	P value
Gender	1.25 (0.38–4.13)	0.70
Age at symptom onset	0.08 (0–7,705,330.35)	0.79
Age at diagnosis	13.17 (0–1,169,765,988)	0.78
Time interval between symptom onset and diagnosis	0.80 (0.17–3.67)	0.77
Subtypes of tic disorder		
Provisional tic disorder	1	0.99
Chronic motor or vocal tic disorder	0.98 (0.22–4.25)	0.98
Tourette syndrome	0.95 (0.06–13.25)	0.97
Initial tic symptoms		
Motor tics	1	0.74
Vocal tics	0	0.99
Motor + vocal tics	1.58 (0.48–5.10)	0.44
YGSS at diagnosis	1.02 (0.97–1.07)	0.39
Presence of neuropsychiatric comorbidities	0.64 (0.19–2.07)	0.46
Treatment utilization	1.12 (0.34–3.66)	0.84

YGSS Yale Global Tic Severity Scale

characterize the demographic and clinical factors influencing the timing of tic disorder diagnosis and clinical outcomes.

We found that the mean age of 6.9 years for the onset of tics was higher than that reported in other studies, which ranged between 4 and 6 years for onset [5–7]. Mild tic symptoms may initially go unrecognized by caregivers and become noticeable only with increasing severity, which may account for the higher mean age at onset in this study. Consistent with previous studies by Robertson et al. [28], we found a higher proportion of tic disorders in males than females in our study. With regard to initial tic symptoms, eye blinking was observed most frequently, accounting for more than half of tic symptoms in patients (50.4%). Previous studies have also noted that tics usually begin in the head and face, with eye blinking being the first and the most common tic [29, 30].

Children with tic disorders have a higher likelihood of concomitant neuropsychiatric conditions [31]. An analysis of shared heritability in 23 different neurologic and psychiatric disorders demonstrated that a significant proportion of polygenic heritability in tic disorders is shared with OCD and ADHD [32]. Our results identified ADHD as the most commonly reported comorbid neuropsychiatric disorder, a finding consistent with previous research [33]. Tics are often not the most enduring or impairing problem in children with tic disorders; other coexisting neuropsychiatric conditions are often a greater source of impairment than the tics themselves [34]. Comorbid ADHD symptoms may have an undesirable impact on social, academic, and behavioral functions

and can negatively impact quality of life and global psychosocial functioning [35–37]. Carter et al. [38] found that children with ADHD and tic disorders have more behavioral problems and poorer social adaptation compared to children with tic disorders only. Moreover, it has been postulated that the presence of ADHD in patients with tic disorders is correlated with higher rates of other neuropsychiatric comorbidities, such as OCD, anxiety disorders, anger control disorders, mood disorders, and personality disorders [5]. Our data noted a similar trend in that children with moderate to severe tics had more co-occurring neuropsychiatric disorders than those with mild tics, although the differences were not statistically significant. At a more general level, our results align with previous research showing that children with tic disorders may have increased healthcare needs and require supplemental mental health or educational services and support [39]. Therefore, clinical assessment of pediatric patients with tic disorders warrants a thorough evaluation for coexisting ADHD and other neuropsychiatric problems.

In our study, a relatively short lag time to diagnosis following the onset of tic symptoms was observed, with a mean duration of 13.3 months. This lag is significantly shorter than the 3 to 8 years delay reported in previous studies [5, 21]. The shorter time to diagnosis identified in our study is comparable to findings from more recent studies [19, 40]. In addition, time lag from when tics were first noticed to diagnosis was negatively correlated with tic severity. Growing awareness of tic symptoms among physicians and the availability of health information to patients and their families may be important factors in shortening the time to diagnosis [19]. Timely

diagnosis of tic disorders may enable patients and their families to have access to optimized medical, psychological, and educational treatment and other support services [40].

We also found that patients with motor tics as the initial manifestation experienced less time to diagnosis than those with vocal tics. Patients with only vocal tics experienced relatively longer times to diagnosis compared to those with only motor tics or combined motor and vocal tics. Because throat clearing, sniffing, coughing, and grunting are the most common types of vocal tics, patients with vocal tics can often be misdiagnosed as having common pediatric conditions such as a cold, asthma, or allergy, which may contribute to diagnostic delay [4, 19].

With regard to follow-up outcomes, the vast majority of patients (83.2%) reported improvement in their tics over time in our study. Tics reach their apex early in the second decade of life and then usually improve during adolescence [30]. According to Bloch et al. [6], more than three-quarters of children with childhood tic symptoms had fewer tics or were completely tic-free at follow-up, while less than a quarter had moderate or greater tics at follow-up. Though questions regarding the clinical predictive factors of follow-up outcomes arise frequently in clinical practice, previous studies have not successfully identified reliable predictors of follow-up outcomes. Prognostic issues can be difficult to address clinically because tic disorders have a complex range of possible symptom combinations and comorbidities [41]. In our study, we attempted to delineate the demographic and clinical factors that could be used to predict the future course of tic disorders. There were, however, no associations between future tic severity and gender, age of tic onset or diagnosis, lag time to diagnosis, subtypes of tic disorders, types of initial tic symptoms, tic severity at diagnosis, presence of neuropsychiatric comorbidities, or treatment utilization. Although we did not uncover robust clinical predictors of the course of tic disorders, our findings may provide a useful platform for further long-term follow-up studies regarding this issue.

Our study is limited by its retrospective nature. Drawing our patient sample from a single referral center likely influenced the lack of statistical significance. Thus, larger prospective studies or collaborative trials are warranted to elucidate the complex interaction of tic severity, comorbidities, and tic-related impairment and reveal the predictors of long-term follow-up outcomes.

Conclusions

The findings of this study suggest that motor tics as the initial manifestation and greater tic severity are associated with a shorter time to diagnosis. Although robust clinical predictors of the course of tic disorders were not identified, our findings extend previous research and provide

potential explanations regarding the clinical features or neuropsychiatric comorbidities that influence the time to diagnosis and predict clinical outcomes in pediatric patients with tic disorders. We also noted heterogeneity in the initial presentation of tics and a higher likelihood of concomitant neuropsychiatric conditions. Thus, this study provides a better understanding and greater insight into the complexities of tic disorders. The evolving nature of tic expression and severity, high prevalence of neuropsychiatric comorbidities, and associated functional impairments reinforce the importance of comprehensive assessment during the disease course for determining and prioritizing goals of treatment. Furthermore, better recognition among parents, teachers, and health care providers of potential challenges related to either tic disorders or co-occurring conditions would help to best support the patient's future health and well-being.

Abbreviations

DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th edition; ADHD: Attention-deficit hyperactivity disorder; OCD: Obsessive-compulsive disorder; YGTSS: Yale Global Tic Severity Scale

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Authors' contributions

The manuscript was written by EGP and YHK. Data collection and analysis was conducted by EGP. YHK supervised all aspects of the analysis and manuscript preparation. All authors have read and approved the final manuscript.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval for this retrospective study was provided by the Institutional Review Board of Catholic Medical Center (IRB UC19RAS10149). The administrative permissions and licenses were acquired by our team to access the data used in our research. Consent to participate is not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that there are no conflicts of interest.

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