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Original Article

Frequency of headache and related clinical factors in children and adolescents with tic disorders

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Abstract

Aim: Only a few studies have investigated the comorbid headache in children with tic disorders (TD). In this study, thus, we aimed to examine the frequency and clinical correlates of comorbid headache in TD.

Material and Methods: The sample consisted of 98 children and adolescents aged 6–16 years with a diagnosis of any tic disorder and 108 healthy children and adolescents matched for age, gender and sociocultural characteristics. All participants underwent a semi-structured psychiatric interview to establish a psychiatric diagnosis. The diagnosis of headache was made according to the third edition of the International Classification of Headache Disorders criteria. Also, a specially prepared personal information sheet and Yale Global Tic Severity Scale were applied.

Results: Children and adolescents with TD had a significantly higher frequency of headache compared to those in the control group (44.9% vs. 22.2%, p=0.001). The most common type of headache in both groups was migraine. We determined that the rate of diagnosis of chronic tic disorders, percentage of the presence of vocal tics, severity of tics, the proportion of patients taking pharmacotherapy for tics, and the rate of psychiatric comorbidity were significantly higher in patients with a headache than those without headache.

Conclusion: The results of our study confirm studies showing suggesting a possible relationship between TD and headache, and supports the proposition that headache is a comorbidity of TD. However, further studies exploring the mechanisms of this relationship are required. It also would be advisable to screen children with TD in terms of headaches.

Keywords: Child/adolescent; headache; migraine; tic disorders; tourette syndrome

INTRODUCTION

Tic disorders (TD) are among the most common motor disorders in childhood and are classified as Tourette syndrome (TS), chronic involuntary motion disorder (chronic motor or vocal tic disorder), temporary involuntary motion disorder. TS is the most common and best defined neuropsychiatric condition characterized by both multiple motor tics and at least one vocal tic, starting in childhood or adolescence, for at least 1 year period (1). Other chronic tic disorder types distinguished from TS by dominance of one tic (which is usually a motor tic) in the clinical picture. Tic disorders lasting less than one year are referred to as temporary tic disorders.

TD's are known to be accompanied by other psychopathologies such as attention deficit/hyperactivity disorder (ADHD), destructive behavioral disorders, anxiety, and obsessive-compulsive disorder (OCD) (2, 3). However, although presence of faint neurological symptoms (4) and increased risk of neurological conditions such as epilepsy (5) have been reported in the studies, relatively little is known about neurological comorbidity. In addition, previous studies have shown that TD may also be associated with headache (6-10). In the studies focusing on the relationship between primary headache disorders and TD, it has been shown that headache rates, especially migraine, are high in those with tic disorder and there is a common etiological pathophysiology shared by the two conditions. In addition, some authors reported that, in their samples very few cases experienced headaches secondary to excessive use of facial or neck muscles due to tics, and thus suggested that headache would be a comorbidity of TD (9). The frequency of tension type headache accompanying TD is reported to vary between 7.3% and 35.5% and frequency of generalized headache is reported to vary between 28.6% and 61.9%, whereas the prevalence of migraine, which is the most researched headache disorder in TD, is reported to vary between 12.9%

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and 43.3 % (11). On the other hand, these rates are almost 4-5 times higher than the rates reported in the pediatric population (12).

The pathophysiology of the increased rates of headache in TD is uncertain, however a number of hypotheses such as common genetic etiologies and a common disorder in the serotonin metabolism and extrapyramidal system have been suggested, and it has been emphasized that obsessive compulsive symptoms may mediate this relationship (13-18). A recent study reporting a common genetic relationship between migraine and TS has been interpreted to be an exciting study (18).

However, in literature, few studies have examined the association between headache and TD and the reports the frequency and features of this comorbidity are contradictory (6-10). A better understanding of the relationship between TB and headache may shed light on possible pathophysiological mechanisms of both tics and specific types of headaches. In addition, evidence-based information on these mechanisms can enable clinicians to develop diagnostic and therapeutic strategies for patients. The aim of this study is investigate the frequency of accompanying headache and related clinical features in children and adolescents with tic disorder.

MATERIAL and METHODS

Participants

The sample of this cross-sectional study consisted of 98 children and adolescents with TD, between the ages of 6-16 and 108 healthy controls matched with the TD group in terms of age, gender, sociocultural characteristics, and educational background. Ethics committee approval was received for this study from the Cumhuriyet University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Decision No: 2019-12/17).Children and adolescents who admitted to the Child-Adolescent Mental Health and Diseases clinic and diagnosed with TD according to DSM-5 criteria (Diagnostic and Statistical Manual of Mental Disorders -5 (DSM-5) were included in the study. Control group consisted of randomly selected healthy children who admitted to the pediatric clinic of our hospital without any known psychiatric disorder, chronic medical disorder, and infection requiring treatment. Those with mental retardation, autism spectrum disorder, and substance abuse, symptoms of mania or psychotic disorder during interview, epilepsy and a history of head injury with loss of consciousness were excluded from the study.

A semi-structured psychiatric interview (Affective Disorders and Schizophrenia Interview Schedule for School-Age Children – Present and Lifetime Version-DSM 5 -Turkish Version (K-SADS-PL-TR) was used to determine any past and present psychopathology in all children and adolescents included in the study (19,20). In addition, a detailed physical examination, neurological examination, blood pressure measurement and ophthalmological examination were performed and detailed history and characteristics of pain were taken from all patients with headache complaints. In the study only children with a diagnosis of tension-type headache (TTH) and concurred migraine as a primary headache diagnosed according to the criteria of International Classification of Headache Disorder, 3rd Edition (ICHD-3) (21) were included. The children with neurological deficits and headaches related to secondary causes (including those attributable to excessive use of facial or neck muscles due to tics and use of psychopharmacology agents) were excluded from the study.

Approval of Ethics Committee of Sivas Cumhuriyet University was obtained before starting the study. Informed consents were obtained from the parents after the purpose and content of the study were explained and all participants agreed to participate in the study. The study was conducted following Good Clinical Practice procedures and the current revision of the Helsinki Declaration.

Data Collection Tools

Personal Information form: It was specially prepared by the researchers by taking into consideration the relevant literature for the purpose of the study. It is an interview form including questions regarding the socio-demographic data of the participants (name, gender, age, place of residence, educational status of parents, monthly income) and the characteristics of tics and headache (duration, frequency, severity, impacts on functionality, and whether any treatment was administered). The parameters in the form were evaluated and filled by the researchers during the interview.

The Yale Global Tic Severity Scale (YGTSS): It is an 11-item scale developed by Leckman et al., in order to evaluate the severity of tic symptoms (22). It consists of two parts. The first part is in the form of a screening list that determines the anatomical distribution of tics. The second part evaluates the number, frequency, severity, complexity and disturbances of tics determined in the first section, in 5 different sub-dimensions ocal tics. The scores that can be obtained from this part of the scale are between 0 and 25, separately for motor and vocal tics and a maximum total of 50. In addition, in this section, the level of disturbance of functionality depending on the effects of tics on the child's self-esteem, family life, social acceptance, friend relationships and school performance is evaluated and scored between 0 and 50 points. As a result, the total score of the scale is between 0-100. Adaptation. Each sub-dimension is scored between 0 and 5 and calculated separately for motor and v of the scale into Turkish and validity-reliability study was performed by Zaimoğlu et al. (23) YGTSS was filled by one-on-one interview technique, depending on the observations and information received from the families.

Statistical Analysis

Statistical data were analyzed by using SPSS 22.0 (IBM Corporation, Armonk, NY, USA). Shapiro-Wilk test was used to evaluate the suitability of the data for normal distribution. Numerical and categorical data are expressed

as mean ± standard deviation (SD), median (min-max), number (n) and percentage (%). Chi-square test was used for categorical variables and Mann-Whitney U test was used for continuous variables. In all tests, a value p <0.05 value was considered statistically significant.

RESULTS

Sociodemographic characteristics of the participants

The study was conducted on 206 children and adolescents, 98 of whom were with TD and 108 were healthy controls. The TD group included 73 (74.5%) boys and 25 (25.5%) girls; the average age was 10.37 ± 2.28 years. The control group included 75 (69.4%) boys and 33 (30.6%) girls; the average age was 10.84 ± 2.24 years. There was no significant difference between the groups in terms of age, gender, place of residence, education level of parents, and income level (p > 0.05 for all). However, when the groups were examined in terms of history of tic disorder, positive family history was found in 18.4% (n = 18) of the participants in the TD group and in 1.9% (n = 2) in the control group; and this difference was statistically significant (p <0.001). The socio-demographic data of the participants are shown in Table 1.

Table 1. Sociodemographic characteristics of the participants

	TD Group (n=98)	Control Group (n=108)	p*
Age (mean-year±SD)	10.37±2.28	10.84±2.24	0.103
Gender (n,%)			
Male	73 (74.5)	75 (69.4)	0.421
Female	25 (22.5)	33 (30.6)	
Place of residence (n,%)			
Urban	62 (63.3)	77 (71.3)	0.219
Rural	36 (36.7)	31 (28.7)	
Income level (n,%)**			
Minimum vage/Below Minimum vage	35 (35.7)	39 (36.1)	0.953
Above Minimum vage	63 (64.3)	69 (63.9)	
Mother's education level (n,%)			
Primary school	29 (29.6)	30 (27.8)	0.774
Higher	69 (70.4)	78 (72.2)	
Father's education level (n,%)			
Primary school	21 (21.4)	22 (20.4)	0.852
Higher	77 (78.6)	86 (79.6)	
History of tic disorder in family (n,%)	18 (18.4)	2 (1.9)	**<0.001**

*Chi Square test, Mann-Whitney U Test. Bold type indicates statistical signficance: p<0.05
**Income levels were calculated based on the minimum vage at the time of the study
SD, Standart deviation; TD, Tic Disorder

Clinical findings, tics distribution patterns and comorbidity rates in the TD group

Clinical findings, distribution patterns and comorbidity rates of TD group participating in the study are summarized in Table 2. The average age of onset of tics was 7.02 ± 1.13 (min-max: 5-10 years). When the cases were evaluated according to type of TD, 68 (69.4%) children had Tourette syndrome, 9 (9.2%) had chronic TD, and 21 (21.4%) had transient TD. None of the children who were diagnosed with chronic TD had chronic vocal tic disorder. Simple motor tics were present in all cases and complex motor tics were present in 64 (65.3%) of the cases. Simple vocal tics were present in 36 (36.7%) of the cases, 9 of them (9.2%) also had complex vocal tics. Nine cases (9.2%) had coprophenoma and 8 cases (8.2%) had echophenoma (Table 2).

A total of 75 (76.5%) TD patients were receiving pharmacotherapy for tics, 15 of them (15.3%) were using antipsychotic as monotherapy, 19 (19.4%) were using combination of antipsychotic and SSRI, 29 (29.6%) were using combination of antipsychotic and atomoxetine, and 12 (12.2%) were using antipsychotic and methylphenidate combination. Based on previous reports, a 35% reduction in YGTSS or an absolute decrease of 6-7 points, with a minimum dose of 8 weeks of appropriate dose for tics was interpreted as response to treatment. Accordingly, we found that, 10 patients (13.3%) were unresponsive to current treatment and 65 (86.7%) responded to treatment (Table 2).

When psychiatric comorbidities were analyzed, it was found that 80 cases (81.6%) had at least one comorbid disorder. The most frequent comorbid diagnoses were ADHD with a rate of 52% (n = 51) and OCD with a rate of 34.7% (n = 34). These were followed by CD-ODD (n = 25, 25.5%), anxiety disorders (n = 17, 17.3%), and depressive disorder (n = 10, 10.2%). In addition, 14 (14.3%) patients had other psychiatric comorbidities (elimination disorders, stuttering, trichotillomania) (Table 2).

Table 2. Clinical findings, distribution patterns and comorbidity rates of TD group

Variables	n	%
Types of TD		
Tourette syndrome	68	69.4
Chronic motor or vocal tic disorder	9	9.2
Transient tic disorder	21	21.4
Motor tics	98	100
Simple Motor Tics	98	100
Complex Motor Tics	64	65.3
Vocal tics	36	36.7
Simple vocal tics	36	36.7
Complex vocal tics	9	9.2
Coprophenoma	9	9.2
Echophenoma	8	8.2
Using medication for tics	75	76.5
Antipsychotic-monotherapy	15	15.3
Antipsychotic-SSRI	19	19.4
Antipsychotic-Atomoxetine	29	29.6
Antipsychotic-Methylphenidate	12	12.2
Response to treatment		
No	10	13.3
Yes	65	86.7
Psychiatric comorbidity*	80	81.6
ADHD	51	52
CD-ODD	25	25.5
OCD	34	34.7
Depressive disorder	10	10.2
Anxiety disorders **	17	17.3
Others ***	14	14.3

*At least one psychiatric comorbiditiy
**Seperation disorder, selective mutism, panic disorder, agoraphobia, generalized anxiety disorder, social phobia, specific phobia
***Elimination disorders, communication disorders, trichotillomania etc.
ACD-ODD: Conduct disorder-Oppositional defiant disorder; ADHD, Attention deficit hyperactivity disorder; OCD, Obsessive compulsive disorder; SSRI, Selective serotonin reuptake inhibitor

Headache assessment

When the study and control groups were evaluated according to "International Classification of Headache Disorder", it was determined that there was a significant difference between the groups in terms of having primary headache in the last 6 months (p = 0.001). Accordingly, 44.9% of the patients in the TD group (n = 44) had primary headache in the last 6 months, while this rate was 22.2% in the control group (n = 24). However, there was no significant difference between the two groups in terms of the type of headache, how long the patients had been suffering, the duration of the pain attacks, its frequency, and the emotional factors that precipitated the pain. The most common type of headache in both groups was migraine (63.6 and 66.7, respectively), while the rate of TTH was 36.4% and 33.3%, respectively, and the majority of cases in both groups had headache for at least 6 months (77.3% and 75%, respectively). The frequency of headache was 1-3 times a month in the majority of the cases in both groups (63.6% and 70.8%, respectively). In terms of emotional factors that precipitate pain, 59.1% (n = 26) of those in the TD group and 41.7 (n = 10) of the control group described at least one emotional factor. When we evaluated whether the pain interfered with daily activities, the majority of those with headache in both groups reported that the pain did not interfere with their daily activities or interfered with some activities (70.5% and 75% respectively). The results of the analysis related to headache are presented in Table 3.

Examination of headache in terms of clinical variables in the TD group

The results regarding the examination of headache in terms of clinical variables are shown in Table 4. There was no significant difference in age and gender between the patients with and without headache in the TD group (p > 0.05). The rate of chronic tic disorders (TS and chronic motor or vocal tic disorder) was significantly higher in the headache group compared to those without headache (95.5% and 64.8%, respectively, p <0.001). In addition a vocal tic was present in 59.1% (n = 26) of headache group, whereas this rate was 18.5% (n = 10) in the group without headache (p <0.001). However, there was no significant difference between the groups with and without headache in terms of the types of motor and vocal tics (simple and complex), coprophenoma and echophenoma (Table 4).

There was also significant difference between the two groups in terms of receiving pharmacotherapy for tics; 88.6% (n = 39) of the group with headache and 66.7% (n = 36) of the group without headache received medication (p = 0.011). However, it was found that the response to drug treatment for tics did not affect the headache (p = 0.089). The rate of patients who responded to the treatment was 79.5% in the group with headache and 94.4% in the group without headache, but the difference was not statistically significant (Table 4).

Again, there was at least one comorbid psychiatric disorder accompanying the group with and without headache. The rate of at least one accompanying psychopathology in the group with headache was 97.7%, while it was 68.5% in the group without headache (p <0.001). We found that, ADHD and OCD were significantly higher in the group with headache (p = 0.038 and <0.001, respectively). There was no significant relationship was between the presence of other comorbid conditions and headache (Table 4).

Table 3. Clinical features of headache

	TD Group (n=98)	Control Group (n=108)	p*
Headache in the last 6 months (n,%)	44 (44.9)	24 (22.2)	**0.001**
Duration of headache complaint (n,%)			
3-6 months	10 (22.7)	6 (25)	0.833
6 months+	34 (77.3)	18 (75)	
Type of headache (n,%)			
Migraine	28 (63.6)	16 (66.7)	0.803
TTH	16 (36.4)	8 (33.3)	
Duration of headache attacs (n,%)			
<60 min	14 (31.8)	6 (25)	0.806
1-2 hours	24 (54.5)	15 (62.5)	
>2 hours	6 (13.6)	3 (12.5)	
Frequency of headache (n,%)			
1-3 in a month	28 (63.6)	17 (70.8)	0.549
At least once a week	16 (36.4)	7 (29.2)	
Precipitating emotional factors for headache (n,%)	26 (59.1)	10 (41.7)	0.169
Interference of headache to daily activities (n,%)			
No interference/ interference to some activities	31 (70.5)	18 (75)	0.690
Interference to all activities	13 (29.5)	6 (25)	

*Chi square test. Bold type indicates statistical significance: p<0.05
TTH, tension-type headache; SS, Standart Deviation; TD, Tic Disorders

Table 4. Relationship between headache and clinical variables in control group

	Headache group (n=44)	Non-headache group (n=54)	p
Age (mean-year±SD)	10.87±2.04	10.49±2.37	0.179*
Gender (n,%)			
Male	32 (72.7)	41 (75.9)	0.718**
Female	12 (27.3)	13 (24.1)	
Type of Tic Disorders (n,%)			
Transient tic disorder	2 (4.5)	19 (35.2)	**<0.001****
Chronic tic disorders (TS and chronic motor or vocal tic disorder)	42 (95.5)	35 (64.8)	
Motor tic type (n,%)			
Simple motor tics	12 (27.3)	22 (40.7)	0.164**
Complex motor tics	32 (72.7)	32 (59.3)	
Presence of vocal tics (n,%)	26 (59.1)	10 (18.5)	**<0.001****
Type of vocal tic (n,%)			0.100***
Simple	19 (73.1)	8 (80)	
Complex	7 (26.9)	2 (20)	
Coprophenoma (n,%)	7 (15.9)	2 (3.7)	0.074***
Echophenoma (n,%)	6 (13.6)	2 (3.7)	0.135***
Using medication for tics (n,%)	39 (88.6)	36 (66.7)	**0.011****
Response to tic treatment (n,%) †			
Yes (partial or complete)	31 (79.5)	34 (94.4)	0.089***
No	8 (20.5)	2 (5.6)	
Psychiatric comorbidity (n,%)	43 (97.7)	37 (68.5)	**<0.001****
ADHD comorbidity (n,%)	28 (63.6)	23 (42.6)	**0.038****
OCD comorbidity (n,%)	21 (61.4)	7 (13)	**<0.001****
CD/ODD comorbidity (n,%)	14 (31.8)	11 (20.4)	0.196**
Depressive disorder comorbidity (n,%)	7 (15.9)	3 (5.6)	0.107***
Anxiety disorders comorbidity (n,%)	9 (20.5)	8 (14.8)	0.463**

*Mann–Whitney U test. **Chi square test. ***Fischer's exact test.
Bold type indicates statistical significance: p<0.05.
†Those who did not receive treatment were excluded from the statistic.
CD/ODD, CD-ODD: Conduct disorder/Oppositional defiant disorder; ADHD, Attention deficit hyperactivity disorder; OCD, Obsessive compulsive disorder SD, Standard deviation; SSRI, selective serotonin reuptake inhibitor; TS, Tourette syndrom

Evaluation of the relationship between the severity of tic symptoms and headache

When we look at the relationship between The Yale Global Tic Severity Scale (YGTSS) scores that we use to evaluate the severity of tic symptoms and headache, the motor tic total scores were 13.57 ± 3.70 and 12 ± 3.15, respectively (p = 0.047); vocal tic total scores were 6.34 ± 6.18 and 2.5 ± 4.90, respectively (p = 0.001); general deterioration scores were 39.32 ± 7.11 and 31.30 ± 9.27, respectively (p = 0.008);and general total scores were 58.98 ± 15.30 and 44.20 ± 14.33, respectively (p <0.001). YGTSS scores were statistically significantly higher in the group with headache in comparison with those without headache. The YGTSS scores of the groups with and without headache are given in Table 5.

Table 5. The relationship between the severity of tic symptoms and headache

	Headache group (n=44)	Non-headache group (n=54)	p*
YGTSS -Motor tic total score	13.57±3.70	12±3.15	**0.047**
YGTSS- Vocal tic total score	6.34±6.18	2.5±4.90	**0.001**
YGTSS -General impairment score	31.30±9.27	39.32±7.11	**0.008**
YGTSS -General total score	58.98±15.30	44.20±14.33	**<0.001**

*Mann–Whitney U test.
Bold type indicates statistical significance: p<0.05.
YGTSS, Yale Global Tic Severity Scale

DISCUSSION

In this study, we evaluated the frequency of headache and associated clinical factors in 98 children and adolescents with TD. The frequency of headache was significantly higher in children with TD in comparison with the control group. In our study, no significant relationship was found between headache and age, sex, presence and type of motor tics, type of vocal tics, coprophenoma and echophenoma, and response to tic treatment. On the other hand, we found that headache is associated with chronic tic disorders (TS and chronic motor or vocal tic disorder), severity of tic, presence of vocal tics, and comorbid conditions; The rate of diagnosis of chronic tic disorders, the percentage of vocal tics, severity of tics, the rate of receiving pharmacotherapy for tics, and the rate of the presence of at least one psychiatric comorbidity were significantly higher in those with headache in comparison with those without headache.

Although, it is well known that, high rates of various psychiatric comorbidities such as ADHD and OCD are seen in patients with TD, very few studies have examined the headache comorbidity in TD. Therefore the data regarding the nature of this comorbidity are still limited (6-10). The studies on this subject revealed that the prevalence of headache, especially migraine-type, was higher in both the child and adult population with TD, in comparison with the general population (6-11,24-26).

Barabas et al. (1984) were first to compare the learning difficulties and epileptic seizure disorders with migraine prevalence in TD patients and showed that the prevalence of migraine was significantly higher in TD patients than those with learning disability and seizure disorder. In this study, conducted on 60 children and adolescents with TD, it was reported that migraine accompanied TD in 27% of the patients (7). Later, in 2003, a study conducted by Kwak et al., on children and adults with TS migraine, migraine was detected in 39% of adults and 16% of children with TD. The prevalence of migraine was found to be significantly higher in both patient groups than in the general population; and the authors concluded that migraine is a comorbidity in TS patients (6). In another study conducted in 2012, on 109 TD patients under 21 years of age, the prevalence of generalized, migraine, and tension types of headache and other headaches were found to be 55%, 17.4%, 28.4%, and 11%, respectively (9). In a study conducted in 2019, on children and adolescents with TD adult patients were compared with children and it was reported that the prevalence of headache was significantly higher in adult patients with TD in comparison with children and adolescents (48.4% vs. 28.6%, p <0.05) (8). In this study migraine was reported to be comorbid in 39% of child patients and TTH was comorbid 16% of child patients (8). In a study conducted in Turkey, it was found that migraine was present in 31.7% of children with TD (10). In a recent review, the frequency of generalized headache in patients with TD was reported between 28.6% and 61.9%, the frequency of migraine was between 12.9 and 43.3%, and tension-type headache was between 7.3% and 35.5 % (11). In our study, headache was found in 44.9% of children with TD and 22.2% of children in the control group. The most common type of headache was migraine in both groups. Our findings are consistent with the results of previous studies suggesting a possible relationship between TD and migraine. In addition, considering that there is no headache secondary to excessive use of facial or neck muscles related to tics, our results support the view that migraine and TTH are comorbidities of TD.

However, studies on clinical correlations of headache in TD have reported contradictory findings. For example, some studies reported that headache in TD patients is not affected by gender, severity of tic, and the presence of psychiatric comorbidities (6,9,10,24), whereas others reported that some of these clinical variables are related

to headache rates (8). In our study, it was observed that headache patterns were affected by the presence of ADHD and OCD as psychiatric comorbidities, and were not affected by the presence of CD/ODD, depression and anxiety disorders. In addition, our findings revealed that headache patterns are not affected by age and gender. In contrast, some studies have reported that headaches are higher in boys than girls, and that this can be explained by the prevalence of TD in the male gender is higher than females at a ratio of 3-5/1 (6,7,9). Therefore, the authors attributed this male dominance to the male sample to a large extent and TS affecting boys more than girls. However, regarding the clinical correlations of headaches in TD, the level of evidence for gender differences was generally found to be weak (6,24,25). In our study, it was also found that age did not affect headache; in our sample the average age of the patients with headache was smaller (approximatly 10-11 years of age) than the average age reported in other studies (approximately 14 and 15 years) (9). This may be due to the low average age of our sample.

More importantly, we found significant relationships between headache patterns and chronicity and severity of tics and presence of vocal tics. However, we found that, coprophenoma and echophenoma, which were suggested to reflect the severity of the disease, were not associated with headache (27,28). This may be due to our small sample size, and it is difficult to draw a definitive conclusion from this result.

Regarding the relationship between the severity of tic and headache, the findings of our study revealed that severity of tics was higher in patients with headache than those without. However, there are contradictory reports from studies regarding the effect of the severity of tic on comorbid headache. Some studies reported that the severity of tic is effective on headache (8), others have not reported such a relationship (24). In general, contradictory findings of different studies have been attributed to methodological differences such as heterogeneity of study populations, variability in data sources, case definitions (sampling and/or reporting bias), and variety of diagnostic criteria (10,11). For example some studies evaluated TS exclusively, whereas others evaluated all types of TD.

In our study, we also found that the rate of receiving pharmacotherapy for tics was significantly higher in the group with headache than those without headache, however the rate of response to treatment was similar. However, the use of psychiatric drugs in our sample is unlikely to affect headache patterns, because secondary headaches that could be attributed to psychopharmacological agents were excluded from our study. Our findings are consistent with the results of Ghosh et al., in 2012 (9). However, whether specific psychiatric drugs will have a causal or therapeutic effect on headache should be addressed in larger prospective clinical trials.

Although the reasons of the high incidence of headache, especially migraine, are not known, in the TD population, it has been suggested that TD and headaches may share a common etiology. In this context, three different hypotheses have been proposed, including the presence of common disorder in the serotonin metabolism, common disorder in the extrapyramidal system, and genetic etiologies common for both migraine and TD (6-8,11,13). A functional neuroimaging study reported that serotonin binding potential, dopamine levels have significantly increased in patients with TD and comorbid OCD in comparison with non-OCD TD patients and healthy controls (14). This finding suggests that that specific TS-OCD phenotypes (ie patients with TS and tic-related obsessive-compulsive behaviors) may be selectively associated with migraine. The significant relationship between the headache pattern in our sample and comorbid OCD also supports this hypothesis. This hypothesis, if confirmed by further studies, can have far-reaching effects for clinical practice, because serotonergic agents used in the treatment of OCD are also beneficial for anxiety and affective symptoms, which are comorbidities of both TD and migraine (8,15). Secondly, a common defect in the extrapyramidal system has also been proposed based on neuroimaging findings demonstrating the involvement of basal ganglia-talamocortical circuits (16,17). Specifically, while functional magnetic resonance imaging provides the strongest finding that indicates to the role of basal ganglia in migraine pathophysiology (16), both structural and functional neuroimaging studies have suggested the basal ganglia to be included in the pathophysiology of TD (17). In addition considering the emphasizing on basal ganglia in the neuropsychology of ADHD (29), the significant relationship between the headache patterns we detected in our study and comorbid ADHD seems to suggest this second hypothesis. Third, more recently, large-scale genetic studies have found evidence for the common heritability of TD and migraine (18,30). The possibility of genetic relationships between TD and migraine should be investigated in further research.

This study has some limitations. First, our findings do not generalize to the community sample and the wider TD population, because the clinic where the research was conducted is a tertiary healthcare institution where more complex and severe TD cases are more probable to be seen. Second, excluding epilepsy, autism, and mental disability, and including only primary headaches in migraine and TTH, may have affected our results. Finally, it was not investigated in this study that, whether these primary headaches were managed properly in TD children would allow the control of tics or other comorbidities. Larger prospective studies are required to answer this question. Despite the limitations, our findings support and extend the results of previous studies investigating the relationship between tic disorders and headache and suggesting headaches as a comorbidity of TD. However, more research is needed to test current hypotheses about the prevalence and clinical correlations of migraine, tension-type headache and other types of headaches in children with TD, and the underlying mechanisms shared between TD and headache.

CONCLUSION

This study is one of the few studies investigating the frequency and clinical correlations of primary headaches as comorbidities in children with TD. The results of our study have confirmed studies indicating that headache is a common problem in children with TD and suggesting that headaches are comorbidities in TD. In our clinical sample, headaches were significantly higher in the children with TD than in the control group, suggesting that screening for headaches and treatment interventions are appropriate in this patient population. If our findings are replicated, it can also guide treatment interventions for clinical practice. For example, pharmacological studies involving drugs such as antiepileptic drug topiramate (18), which are effective in treating both headache (migraine prophylaxis) and TD (tic control), can be conducted. As a result, a better understanding of the relationship between headaches and tics can help the characterization of TD phenotypes and improve diagnostic and treatment strategies.

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