Prevalence of Potential Essential Tremor Cases in Turkish Adolescents According to The WHIGET Classification

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ABSTRACT

Objective: Essential tremor is the most common movement disorder diagnosed during adolescence. However, there are insufficient data about its prevalence among adolescents. This study aims to determine the prevalence of potential essential tremor cases in Turkish adolescents.

Materials and Methods: This cross-sectional study was carried out in Istanbul, Turkey. A total of 5 high schools were visited. In the first step, the authors provided 5559 students (aged 14-18) with clinical information about tremors and essential tremors in their classrooms. After that, a 12-item questionnaire filled by adolescents and parental consent forms were collected. The response rate was 78% (n = 4330). According to the questionnaire answers, adolescents who complained of experiencing tremors in any part of their body were clinically evaluated in the second step of the study. Lastly, a neurological examination to classify essential tremors based on the Washington Heights Inwood Genetic Study of Essential Tremor (1998) diagnostic criteria was conducted by a specialist.

Results: The prevalence of tremor in the respondents aged 14-18 (median = 15) years was 1.2% (n = 52/4330), and the prevalence of essential tremor was 0.41% (n = 18/4330). Male to female ratio for essential tremor was 5:1 (male = 15 and female = 1). Essential tremor cases were subclassified as following: 10 (55.5%) definite essential tremor, 3 (16.6%) probable essential tremor, and 5 (27.7%) possible essential tremor.

Conclusion: The data support the claim that essential tremor is a prevalent movement disorder in Turkish adolescents.

Keywords: Prevalence, tremor, essential tremor, adolescents

INTRODUCTION

Essential tremor (ET) is the most common movement disorder in the world.1 It is characterized by a postural tremor with or without kinetic tremor.1-3 There are insufficient epidemiological data about its prevalence during childhood and adolescence.4-5 Although the likelihood of the disease increases proportionally with age, studies on adults point to childhood as the period when symptoms start.6-8 There is a positive correlation between positive family history and the early onset of tremor.9

The prevalence of ET in all age groups worldwide ranges from 0.9% to 6%.10-13 Epidemiological data on ET in childhood are limited. The prevalence is reported to be 5% in adolescents based on clinical studies, and the onset age of tremor in childhood has not been identified.13-14 Epidemiological data vary according to the population’s socio-demographic characteristics and the geographic region where the study has been conducted.

What is already known on this topic?

- Essential tremor (ET) is the most common movement disorder diagnosed during adolescence.
- Although the likelihood of the disease increases proportionally with age, studies on adults point to childhood as the period when symptoms show.
- However, there are insufficient data about its prevalence among adolescents.

What this study adds on this topic?

- This research is the first epidemiological study documenting pediatric ET prevalence in Turkey.
- The findings of this study support that ET is a common movement disorder in adolescents.
- There is a need for clinical and epidemiological studies with long follow-up for ET not only among adults but also among children and adolescents.
Although there are no community-based surveys specific to childhood and adolescence, one study has included the childhood period.\textsuperscript{15} In particular, there are no epidemiological or clinical studies on the prevalence of ET among Turkish children and adolescents. This study aims to estimate the prevalence of ET in the Anatolian side of Istanbul, Turkey, in adolescents aged 14–18 years old.

**MATERIALS AND METHODS**

**Study Design and Setting**

This cross-sectional study was conducted between September 2016 and June 2017 in Istanbul, Turkey. In total, 5 high schools were visited: 4 in Kadıköy district (population = 451 453) and 1 in Ataşehir district (population = 423 372). The survey aimed to include all students from the 8th to 12th grade (aged 14–18).

The prevalence of ET in all age groups worldwide is 0.3%–6%, and the prevalence of ET in adolescents is 5% in clinical studies. The research sample was calculated as a minimum of 2500 adolescents with a 95% CI, 1.5 pattern effect, and a 5% margin of error. Since there is no epidemiological study in adolescents, all adolescents who are accessible were included in the study (n = 5559).

The study was divided into 3 steps: (1) distribution of parental consent forms and questionnaire to be filled by adolescents, (2) assessment of adolescents with tremor complaints once by a pediatrician, and (3) assessment of adolescents with suspected ET once by a pediatric neurologist. Adolescents were examined once in their schools at all stages and laboratory testing could not be performed due to fieldwork.

**Participant and Data Collection**

The first phase of the study involved the first author (NYS) visiting 5 high schools and giving clinical information about tremors and ET and the aims of the study. A screening questionnaire to be filled out by adolescents and parental consent forms was given to all students (n = 5559) between the ages of 14 and 18, excluding those who did not attend school on the day of the survey. Therefore, the coverage rate was above 95%. A questionnaire consisting of 12 questions (Table 1) administered in the Turkish language inquiring about sociodemographic characteristics, tremor symptomatology, duration, family, and medical history was prepared. The purpose of the questionnaire was to investigate the diagnostic criteria of ET which was adapted by Doğu et al\textsuperscript{6} The overall response rate was 78% (n = 4330) (Figure 1).

Participants with complaints of tremors in any part of the body were selected for the second phase. During the second phase, the participants were assessed once by the first author. Detailed anamnesis and physical and neurological examination findings were recorded (Table 2).

At the final phase, tremor cases diagnosed during the second phase were re-evaluated with a neurological examination by the second author, a pediatric neurologist. Definite and differential diagnoses of ET were done according to the Washington Heights Inwood Genetic Study of Essential Tremor (WHIGET) diagnostic criteria.\textsuperscript{7} The tremor examination included testing for postural, kinetic, isometric, static, and sound tremor.

**Table 1. Essential Tremor Questionnaire Filled Out by Adolescents (Step 1)**

| Question                                                                 | Response Options |
|-------------------------------------------------------------------------|------------------|
| 1. Age:                                                                 |                  |
| 2. Gender: (1) Male (2) Female                                          |                  |
| 3. Do you have tremor? (hand, foot, voice, head, chin)                  | (1) No (2) Yes   |
| 4. Do you have tremor at rest?                                          | (1) No (2) Yes   |
| 5. Does your tremor increase when you get excited?                      | (1) No (2) Yes   |
| 6. Do you have tremor when you stretch your hands and arms?             | (1) No (2) Yes   |
| 7. Do you have tremor while carrying a tray or similar activities       | (1) No (2) Yes   |
| 8. When did your tremor start? (duration of tremor?) day …month …year   |                  |
| 9. Is there anyone in your family who has tremors? (family and/or siblings) | (1) No (2) Yes |
| 10. Do your parents come from the same family?                           | (1) No (2) Yes   |
| 11. Do you have any illnesses? Is there any drug you use?               | (1) No (2) Yes   |
| 12. Is there anyone in your family who has tremors? (close relatives)   | (1) No (2) Yes   |

Thank you for filling out our questionnaire.
(1) Static tremor: it is evaluated by supporting the arms against gravity and in the absence of voluntary muscle contraction. (2) Postural tremor: it is evaluated with the arms extended forward. (3) Kinetic tremor: water transfer; drinking water from a glass; drinking water with a spoon; finger–nose test; evaluated by drawing a spirogram. (4) Isometric tremor: evaluated by making fists. (5) Voice tremor: assessed by speech.

The severity of the tremor was quantified based on the WHIGET tremor rating scale which was used in field studies in our country and defined a total tremor score (range from 0 to 36, with a rating of 3 on 12 tests). In addition, other forms of tremor were differentiated. Dystonic tremor was ruled out based on the following reasons: (1) absence of dystonia in the limb with tremor, (2) rhythmicity of the tremor, and (3) lack of neutral point or limb posture with tremor improvement or disappearance. Psychogenic tremor was ruled out based on the following criteria: (1) no history of sudden onset, (2) absence of underlying psychologic or psychiatric predisposition, and (3) lack of other features like entertainability, variability, suggestibility, and distractibility. The tremor was amplified in different scenarios: (1) while doing various postures like outstretched arm with forearm supinated and pronated with eyes closed, arms ab ducted with elbows flexed to bring the fingers close to each other in front of the chest with eyes closed, raising arms above
head with forearm supinated and pronated; (2) while drawing an Archimedes spiral, a line, and handwriting; and (3) while pouring water from one cup to another and during the use of a spoon.

**Statistical Analysis**

Data were analyzed using the Statistical Program for the Social Sciences version 20.0 (IBM, Armonk, NY, USA). Sociodemographic data were expressed as mean and standard deviation/median and interquartile range for continuous variables and counts (n) and proportions (%) for descriptive variables.

**Ethical Consideration**

The ethics committee approval was obtained from Marmara University, School of Medicine Ethics Committee (Date: July 15, 2016, Protocol number: 09.2016.411). To conduct the study in schools, further approval was obtained: first, from the Kadıköy District Directorate of National Education and District Governor (article number: 28.09.2016/40537843-136-E.10429549), then from the Istanbul Provincial Directorate of National Education and the Provincial Governor (article number: 20.04.2017/59090411-44E.5465343).

**RESULTS**

The age distribution of the student respondents was between 14 and 18 (median = 15). The overall response rate, male 1691 (39%) and 2639 female (61%), was 78% (n = 4330) students. While 344 (7.9%) of the complaints of tremors were detected, 9 (2.6%) were excluded: 1 patient had obsessive–compulsive disorder, 2 had depression, 3 had anemia (B12-Fe), and 3 had goiter. Out of 335 cases (7.7%) with tremor complaints in different parts of the body neurological examined at the first evaluation, tremor was detected in 52 (15.5%) with slight male predominance (n = 29, 55.2%). A total of 34 (65%) cases included in the second evaluation were evaluated as psychogenic tremors and 18 (34.6%) as ET. The prevalence of tremor was 1.2 % (n = 52/4330), and the prevalence of ET was 0.41% (n = 18/4330). Cases were defined as “definite, probable, and possible.” These definitions are not according to any formal source. We assumed “definite cases” to be the cases diagnosed by the pediatric neurologist; “probable case” to be the cases diagnosed by a general pediatrician; and “possible cases” to be the suspected cases according to questionnaires filled out by adolescents. When the cases (n = 18) were subclassified, 10 cases (55.5%) were evaluated as definite ET, 3 (16.6%) as probable ET, and 5 (27.7%) as possible ET. Majority of the cases (15 male, 83.3 %) (male [n = 15] to female [n = 3] ratio was 5 : 1) diagnosed with ET involved males (Table 3).

**Tremor Characteristics**

Hand tremor was detected in all cases. When the family history was questioned, 5 cases (27.7%) identified at least 1 relative with similar complaints. In the family history, only 2 cases (11.1%) (1 of mother and 1 of brother) were diagnosed with ET without receiving any treatment. Stress was the major exogen factor in cases of increasing severity of the tremor. When the daily activities of the cases were questioned, only 4 cases (22.2%) stated that the symptoms affected them. When the onset time of the symptoms was questioned, only 1 case indicated a period of 5 years, while 12 cases did not give a definite period (66.6%). None of the cases were referred to secondary or tertiary care hospital (Table 3).

**DISCUSSION**

Based on our results, we found that the prevalence of tremor and ET among adolescents was 1.2% and 0.41%, respectively. The male to female ratio was high (5 : 1) and showed that males were more likely to experience ET in comparison to females. The prevalence of ET nationwide is estimated to be 3%-4% in individuals aged 17 years and above. Overall, related literature shows the prevalence of ET among all ages ranging from...
According to the latest classification of ET, the duration of tremor is one of the main limitations in the pediatric population.1-2 The latest consensus statement on the classification of tremors included at least 3 years as the duration of ET.1-2 Tremor lasting less than 3 years but fulfills the criteria for ET should be labeled as the observation period as indeterminate tremor. Ghosh et al3 stated that the duration of tremor should not be than 3 years but fulfills the criteria for ET should be labeled in the adolescence period, the rate of ET localized to hands has been detected. In numerous clinical studies where the distribution of tremor according to anatomical regions was examined, a specific underlying gene has not been discovered yet; recent reports link LINGO1, FUS, and TENM4 to ET.25-26

Gender distribution of ET in our study showed predominance among males (male = 15) to females (n = 3) ratio was 5:1 although the number of females (n = 1691 (39%) male, n = 2639 (60%) female) in the study population was prominently high. Increased male to female prevalence ranging from 1.3 to 2.1 was previously reported in similar age groups.23 In a population study, Mancini et al4 reported that among all age groups, males had a 50% greater risk for tremor or ET than females (male/female ratio = 1.5 for all age class). A recent meta-analysis showed that even after controlling for age, ET was more common among males and that this is more apparent in the pediatric population.27-28 Another study explained that certain genetic and hormonal influences, which are yet to be known, may play a role in determining the body region that is most affected by the tremor.29 In our current study, only hand tremor was detected. In numerous clinical studies where the distribution of tremor according to anatomical regions was examined in the adolescence period, the rate of ET localized to hands has been reported to be 90%-100%.23-24

In conclusion, the result of this study supports the claim that ET is not a rare movement disorder in adolescents. Clinical and epidemiological studies with long follow-up for ET among children and adolescents are required.

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