

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

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What is already known on this topic?

- Essential tremor (ET) is the most common movement disorder diagnosed during the adolescence period.
- 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.

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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 İstanbul, 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.

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Although there are no community-based surveys specific to childhood and adolescence, one study has included the childhood period.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 0.9%-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 al¹⁶ 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.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)

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 (drinking water, using cutlery, etc.)?
(1) No (2) Yes
8. When did your tremor start? (duration of tremor?) ...day ... week ...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.

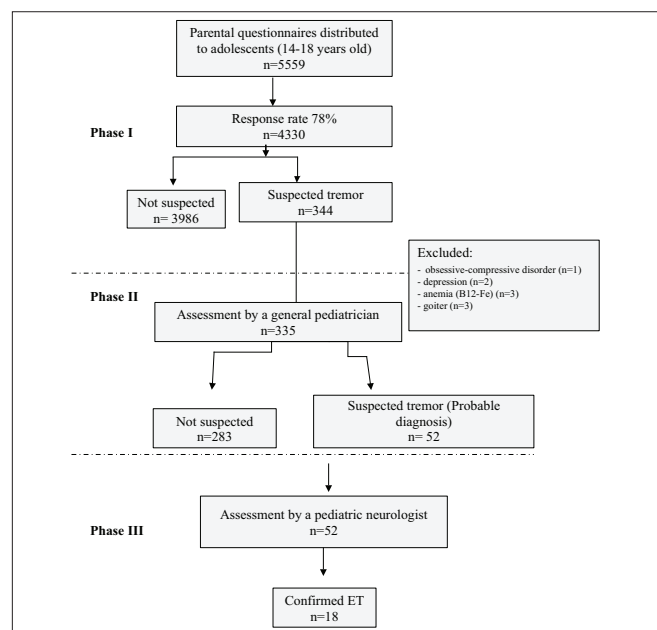

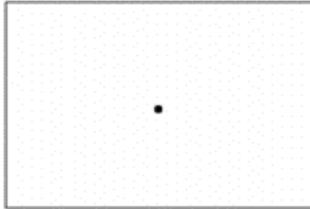


Figure 1. Flowchart showing patient distribution according to the study protocol. Suspected diagnosis: cases included following the assessment of questionnaire responses. Probable diagnosis: cases evaluated (anamnesis, physical examination, and tremor assessment) by a general pediatrician. Confirmed diagnosis: cases re-evaluated by a pediatric neurologist.

Table 2. Physical Examination Paper (Step 2)	
Code: Age: Gender: School:	Resume: Family history: Short anamnesis
Physical examination: Neurological examination: Evaluation (evaluated by postural 1, kinetics 5 tasks) 1- Static tremor: evaluated by supporting the arms against gravity and in the absence of voluntary muscle contraction. 2- Postural tremor: 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 with making fists. *Voice tremor: assessed by speech. Tremor scan questions; 1-Do you have tremor? (hand, foot, voice, head, chin) 2-Do you have tremor at rest? 3-Does your tremor increase when you get excited? 4-Do you have tremor when you stretch your hands and arms? 5-Do you have tremor while carrying a tray or similar activities? (drinking water, draining water, using cutlery, etc.)? 6- When did your tremor start? 7- Does anyone in your family suffer from tremors? 8- Do your parents come from the same family? 10-Do you have any illnesses? Is there any drug you use? 11- Is there anyone in your family who has tremors? (close relatives) 12- Can draw circles from the inside out, starting from the point in the empty box? <div style="display: flex; justify-content: space-around; align-items: center;">   </div>	

(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: hands are 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).⁷ 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 abducted with elbows flexed to bring the fingers close to each other in front of the chest with eyes closed, raising arms above

Table 3. Characteristics of Cases with Essential Tremor Diagnosis

	Gender	Age	Result	Duration	Similar Complaint/ET History in the Family
Case 1	Male	17	Definite ET		
Case 2	Male	17	Definite ET	5 years	Sister/hand
Case 3	Male	15	Definite ET		
Case 4	Male	16	Definite ET		Grandfather/hand
Case 5	Male	16	Definite ET		Cousin /hand
Case 6	Male	14	Definite ET		
Case 7	Female	14	Definite ET	3 months	
Case 8	Male	16	Definite ET	1 year	
Case 9	Male	17	Definite ET	3 years	
Case 10	Male	17	Definite ET		Brother/hand
Case 11	Female	16	Probable ET		
Case 12	Male	15	Probable ET	1 month	
Case 13	Male	16	Probable ET	1 year	
Case 14	Male	16	Probable ET		
Case 15	Female	14	Probable ET		
Case 16	Male	14	Possible ET		
Case 17	Male	17	Possible ET		
Case 18	Male	17	Possible ET		Mother/hand

ET, essential tremor.

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.1042 9549), 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.¹⁷ Overall, related literature shows the prevalence of ET among all ages ranging from

1%–3% in epidemiological studies,^{8,10–13,17–22} to 1%–4% in clinical studies.^{23–24} However, epidemiological data are very limited in children and adolescents.

According to the related literature, family history is prevalent and important in ET diagnosis and clinical presentation. In numerous studies, the diagnosis of ET in first-degree relatives in the family was reported as 50% on average.^{4,24} In this study, 2 patients (11.1%) had a diagnosis of ET in their family history. 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 (n = 15) to female (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 al⁸ 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%.^{9,23–24}

According to the latest classification of ET, the duration of tremor is one of the main limitations in the diagnosis of pediatric ET, especially in epidemiological surveys.^{1,30–31} 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 during the observation period as indeterminate tremor. Ghosh et al³¹ stated that the duration of tremor should not be used as a criterion among children and adolescents, as it is harder to recognize symptoms and their onset. In this study, the WHIGET diagnostic criteria proposed by Louis et al⁷, which excludes the duration of symptoms for the diagnosis of ET, was utilized.⁷ In pediatric studies, the selection of ET cases was based solely on the clinical core diagnostic criteria.^{30–31} Other secondary diagnostic criteria, such as family history or suppression with alcohol, are also inapplicable to children, hence were not used.^{7,31}

This study included a large sample size, improving the statistical power of the results. Thus far, this research is the only study documenting pediatric ET prevalence in Turkey and also one of the limited numbers of studies on the prevalence of ET in adolescents all around the world.

However, there are several limitations in our current study; first, being a cross-sectional study, the findings are limited to a specific population at a specific time and cannot be generalized to other countries or times. Nevertheless, this can contribute further evidence concerning the prevalence of ET in children and adolescents. Second, being a field study, long-term

clinical follow-up of patients and evaluation of the persistence of symptoms were not possible. Finally, obtaining a family history from students instead of the use of medical records, radiologic, or laboratory findings may give rise to recall bias.

CONCLUSION

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.

Ethics Committee Approval: This study was approved by the Ethics Committee of Marmara University, (Approval No: 09.2016.411).

Informed Consent: Written and verbal informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.Y.S., D.T.; Design – N.Y.S., D.T.; Supervision – D.T.; Resources – N.Y.S., D.T.; Materials – N.Y.S., D.T.; Data Collection and/or Processing – N.Y.S., D.T.; Analysis and/or Interpretation – N.Y.S., D.T.; Literature Review – N.Y.S., D.T.; Writing Manuscript – N.Y.S., D.T.; Critical Review – N.Y.S., D.T.

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