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Research Article

Clinical Characteristics of Essential and Physiological Tremor in Orhangazi District of Bursa, Turkey: A Population Based Study

Sevda ERER¹, Mehmet ZARİFOĞLU¹, Necdet KARLI¹, Alis ÖZÇAKIR², Cigdem ÇAVDAR¹, Gökhan OCAKOĞLU³

¹Uludağ University School of Medicine Department of Neurology, Bursa, Turkey ²Uludağ University School of Medicine Department of Family Medicine, Bursa, Turkey ³Uludağ University School of Medicine Department of Biostatistics, Bursa, Turkey

Summary

To find out the estimated prevalence and clinical features of tremor and its subtypes, such as essential tremor (ET) or physiological tremor (PT), by means of a population-based study in the Orhangazi district of Bursa, Turkey.

Our study was carried out between June 2004 and September 2005 among adults aged 40 years or more in Orhangazi, Bursa, Turkey. This population-based study was planned in 3 phases. In phase 1, face-to-face home interviews with 1124 subjects were carried out by residents of the departments of neurology and family medicine, using a short questionnaire; 247 persons had symptoms indicative of tremor. Of the persons with tremor symptoms in phase 1, 48 did not continue to phase 2. In phase 2, participants were videotaped and evaluated by movement disorders specialists by using scales specific to tremor. In phase 3, video recordings of all identified patients were reviewed and final diagnoses were made through a consensus of all three specialists.

In the study population, the prevalence rate of ET was found to be 3.34%; of PT, 4.14%; and all types of tremor, 9.00%. There was no significant variability according to gender and age groups in prevalence rate of ET, PT. ET and PT showed significant comorbidity with hypertension (HT), rheumatological disease, diabetes mellitus (DM), and asthma.

Key words: Tremor, movement disorders, prevalence

Türkiye Bursa İli Orhangazi İlçesinde Esansiyel ve Fizyolojik Tremorun Klinik Özelliklerinin Araştırılması (Toplum Tabanlı Çalışma)

Özet

Toplum tabanlı yaptığımız bu çalışmada, Türkiye'nin Bursa ili Orhangazi ilçesinde esansiyel tremor ve fizyolojik tremor gibi tremor alt tiplerinin prevalans oranlarını ve klinik özelliklerini ortaya koymayı amaçladık.

Çalışmamız, Haziran 2004- Eylül 2005 yılları arasında Bursa Orhangazi ilçesinde yaşayan 40 yaş ve üzeri erişkinler üzerinde yapıldı. Üç fazlı olarak planlanan çalışmamızda, faz 1'de 1124 olgu aile hekimliği ve nöroloji asistanları tarafından kısa anket formları kullanılarak kapı-kapı ev ziyaretleri şeklinde tarandı. Faz 1'de taranan kişilerin 247'sinde şüpheli tremor saptandı, 48 kişi faz 2'ye katılımı kabul etmedi. Faz 2 de bu olgular, hareket bozukluğu ile ilgilenen uzmanlar tarafından değerlendirildi, tremor skalaları doldurularak video kayıtları alındı. Faz 3'de tüm olguların video görüntüleri uzmanların ortak görüşleri doğrultusunda tekrar değerlendirildi ve kesin tanı konuldu.

Bu çalışmada Esansiyel tremor prevalansı % 3.34, fizyolojik tremor prevalansı 4.14%; ve diğer tremor alt tipleriyle birlikte tremor prevalansı % 9.00 olarak bulundu. Esansiyel, fizyolojik tremor prevalans oranlarında yaşa ve cinsiyete göre anlamlı bir değişkenlik saptanmadı. Esansiyel ve fizyolojik tremorla birlikte kronik hastalıklardan hipertansiyon, romatizmal hastalıklar, diyabet ve astımın istatistiksel olarak anlamlı komorbiditesi saptandı.

Anahtar Kelimeler: Tremor, hareket bozuklukları, prevalans

INTRODUCTION

Tremor, an involuntary oscillation of a body part, can be classified into several types: rest, postural, and kinetic tremors. Essential tremor (ET), the most common adult tremor, is primarily an autosomal dominant disease characterized by postural and kinetic tremor of body parts without other neurological signs⁽²⁴⁾. However, abnormalities in tandem gait, ataxic gait, and broad-based gait have been observed in patients with ET⁽²¹⁾. Physiological tremor (PT) may occur in every normal individual but may be exacerbated by strong emotional disturbances (such as anxiety or fear) or certain medical conditions. Enhanced PT is a strengthening of physiologic tremor through more visible levels. It is generally caused by reaction to certain drugs, alcohol withdrawal, or medical conditions including an overactive thyroid and hypoglycemia. It is usually reversible once the cause is corrected⁽¹⁾.

The published prevalence of ET shows considerable variation among studies, largely due to differences in methodology, demographic characteristics, and age strata studied. Reported prevalence in Asian countries varies between 0.015% and 1.59%^(5,12,23), while that in European and American countries is in the range of 0.4% to 22%^(3,8,17).

Underestimation of the actual prevalence rate may be a consequence of tremor symptoms not being taken into account by patients, or being overlooked by physicians. Considering the adverse effects of tremor symptoms on quality of life, we believe that prevalence studies could play an important role in early diagnosis and treatment. Therefore, in the present study,

we aimed to establish and to report the clinical features and prevalence of subtypes of tremor in Orhangazi District of Bursa.

MATERIAL AND METHODS

Bursa, with a population of 2,125,140 according to the 2000 census, is industrially and socioeconomically developed, and is the fourth largest city in Turkey. Orhangazi district, where the study was conducted, has a population of 44,426. Our study population included both rural and urban regions of the Orhangazi district.

The study was carried out between June 2004 and September 2005 on adults aged 40 and older living in Orhangazi district. Based on 2000 national census data, we predicted that, in 2004, people aged 40 years and older comprised 35.3% (36.2% women, 34.4% men) of the total population of Bursa and 27.2% (26.6% women, 27.7% men) of the total population of Orhangazi.

The anticipated prevalence of movement disorders was 15% for sample size calculation range^(3,9,13,15,16,18-20,22). Sample size n was calculated using the following formula, where N is the size of the population, Z is the Z statistic for 95% confidence level, n is sample size, p is the probability of occurrence and d is the precision⁽¹¹⁾.

$$n = NZ^2 p(1 - p) / d^2 (N - 1) + Z^2 p(1 - p)$$

Using this equation for calculation, field screening of 1256 persons 40 years of age and older was considered sufficient to identify patients with movement disorders with 2.0% sensitivity.

A multistep, stratified, cluster sampling method was used for subject selection. In the first step, the number of persons aged 40 years and older living in each subsection of the Orhangazi district was calculated. The study population gender ratio was also adjusted according to the population gender ratio in Orhangazi. Random sampling was done among these sections according to the proportional size of the age groups. The first street in each section to be included in the study was chosen blindly by drawing a tag with the name of the street written on it. Houses odd-numbered in the first street were visited first, followed by even-numbered houses in numerical order. New streets were determined by drawing until the number of potential participants for that section was reached. When the required number of participants was enrolled, our researchers moved on to the next section and used the same method.

In the pre-study period, all screening researchers received a one-day clinical education course on movement disorders. The study was planned in 3 phases. In phase 1, all participants were visited at their homes and screened face-to-face by 3 family medicine and 3 neurology residents. During this screening phase, participants answered a short questionnaire regarding movement disorders. Participants who answered at least one question in this questionnaire positively were selected for phase 2 screening (Figure 1).

In phase 2, participants with symptoms indicative of tremor were assessed by movement disorder specialists and videotaped; those participants with findings of tremor symptoms were asked to answer a 22-item movement disorder screening form (Figure 2).

In the present study that was planned to evaluate the prevalence by scanning

general movement disorders, we aimed to determine sub-types and clinical features of tremor. We used the inclusion and exclusion criteria set forth in the Guidelines of the Ad Hoc Scientific Committee to establish ET diagnosis⁽⁷⁾. Psychogenic tremor was diagnosed on the basis of historical and clinical diagnostic criteria⁽²⁵⁾, and the clinical descriptions of Bhidayasiri R. were used to diagnose physiological tremor⁽⁶⁾.

In phase 3, three movement disorder specialists (MZ, NK, SE) reviewed the video records of the participants who had received a movement disorder diagnosis in phase 2. All three specialists have been running movement disorders outpatient clinics for 10, 5, and 4 years, respectively. For definite diagnosis, agreement of all movement specialists on the same diagnosis was required.

The study was approved by the Local Ethics Committee of Uludag University and was performed in accordance with the latest version of Declaration of Helsinki. All participants gave informed consent prior to their inclusion in the study.

Statistical Analysis

Statistical analyses were carried out using the SPSS v11.0 for Microsoft Windows statistical package (SPSS Inc., Chicago, IL, USA). All continuous variables are expressed as mean \pm standard deviation (SD), and all categorical variables are expressed in terms of frequency (n) and percentage (%). The crude prevalence rate, and age- and sex-adjusted prevalence rates were calculated using weighting and imputation procedures. The Pearson's chi-square test and the Student's t-test were employed to make comparisons. A p-value <0.05 was considered statistically significant.

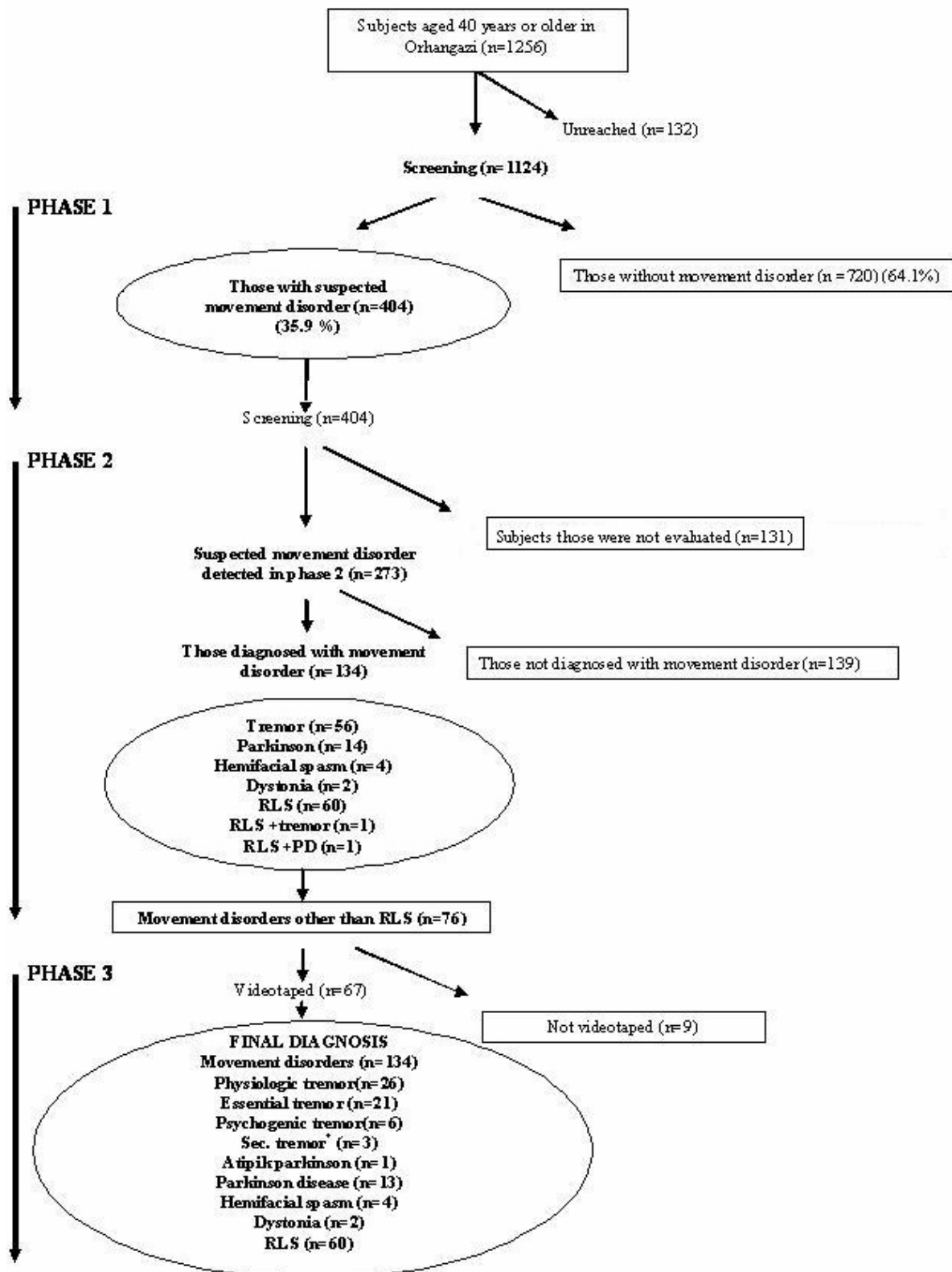


Figure 1: Flowchart of the study. RLS: Restless leg syndrome, PD: Parkinson's disease. Sec. Tremor: Secunder tremor.

Movement Disorders Screening Form

1. Patient's name:
2. Age (years):
3. Handedness:
4. Sex:
5. Family history of movement disorders:
6. Duration of tremor:
7. Co-existence of movement disorders:
8. Disability related to movement disorders:
9. Drug induced exacerbating factors for movement disorders:
10. Initial symptoms: Tremor Rigidity Bradykinesia Pain Vertigo
11. Side of initial findings: Right Left Bilateral
12. Neurological examination: Paresis Pathological reflexes
13. Tremor: 0:None 1:mild 2:moderate 3:marked 4:severe
14. Rigidity: 0:None 1:mild 2:moderate 3:marked 4:severe
15. Anteflexion posture: + -
16. Dystonia: 0 1:Orolingual 2:Head-neck 3:Hand 4:Arm 5:Leg 6: Trunk
17. Hemifacial spasm: + -
18. Hoehn-Yahr score:
19. Tremor severity rating:

Location	Rest	Postural	Kinetic	Total
Face/tongue-chin				
Voice				
Head-neck				
Trunk				
Right arm				
Right hand				
Left arm				
Left hand				
Right leg				
Right foot				
Left leg				
Left foot				
Task-specific				

20. Drawings: 0:Normal 1:Slightly abnormal 2:Moderately abnormal
 3:Markedly abnormal 4:Severely abnormal
- a) Spiral Right hand Left hand
- b) Draw straight line Right hand Left hand
21. Handwriting: 0:Normal 1:Slightly abnormal 2:Moderately abnormal
 3:Markedly abnormal 4:Severely abnormal
- Handwriting sample:
22. Speaking and voice rating: 0:Normal 1:Slightly abnormal 2:Moderately abnormal
 3:Markedly abnormal 4:Severely abnormal

Figure 2: Movement Disorders Screening Form

RESULTS

Of the 1256 persons screened in phase one, 1124 (89.6%) were included in the study, whereas 132 persons did not participate. The mean age (\pm SE) of the 1124 persons screened in phase 1 who participated in the study was 57.8 ± 0.3 years (range: 40-95 years). Of those, 574 were female (51.1%) and 550 were male (48.9%), with mean (\pm SE) ages of 56.6 ± 0.4 years and 59.8 ± 0.5 years, respectively.

In phase one, 404 (32.2%) persons with indications of a movement disorder were identified (Figure 1); 273 were invited for phase 2, but 131 were not invited in phase 2. The reasons for the assessment failure for some subjects in phase 2 were their unwillingness to participate in the study and inability to locate them in the given addresses. There were no statistically significant differences between the persons who participated and the persons who did not participate in the study in terms of age and presence of chronic diseases ($p > 0.05$). However, the ratio of males among the persons who did not participate in the study was significantly higher than those of included in the study ($p < 0.001$). Therefore, we adjusted our crude prevalence rate age and sex-adjusted prevalence rates using weighting and imputation procedures for the 1124 persons who participated in the study rather than the 1256 persons originally screened in phase 1.

Among phase 1 participants, 247 cases of possible tremor were identified, 48 of which could not be assessed. Hundred and ninety nine participants with indications of tremor were evaluated by the movement disorders specialists in phase 2, and 56 (28.1%) were diagnosed with tremor. Among these, 26 participants had PT, 21 had ET, 6 had psychogenic tremor, 2 had tremor secondary to hyperthyroidism and 1 had post-stroke tremor (Figure 1). The mean age (\pm SD) of the persons diagnosed with tremor was 59.8 ± 10.3 years.

When the patients were reassessed using video recordings in phase 3, there were no discrepancies in regard to the diagnoses made in phase 2; only a few differences in tremor subtypes were noted. None of the patients diagnosed with ET had consulted a physician about these symptoms before the study nor had received any treatment for the symptoms.

The crude estimated prevalence of ET, PT, and all types of tremor among persons those 40 years and older was 3.34%, 4.14%, and 9.00%, respectively (Table 1). Among the age groups, the prevalence of ET was observed to be higher among 50- to 59-year-old patients (6.16%) and among patients who were 70 years and older (9.13%) compared to other age groups. It was 4,51 % for 60-69 year old patients. The prevalence of PT was observed to be higher among patients aged 70 years and older (6.09%) compared to other age groups. The prevalence was 2,89 % among 40-49 years old patients, 4,93 % among 50-59 years old patients and 5,41 % among 60-69 years old patients. The prevalence rate of all types of tremor was 3,97 % among 40-49 years old patients, 11,71 % among 50-59 years old patients, 12,63 %, among 60-69 years old patients and 18,26 % among 70 years and older. However, ET, PT, and all types of tremor prevalence rates did not show any statistically significant difference across age or gender groups (Table 1). ($p > 0.05$).

Comorbidity of high blood pressure, rheumatological diseases, diabetes and bronchial asthma with ET and PT was significant ($p < 0.05$). Use of beta-blockers, calcium channel blockers, and oral antidiabetics (to treat diseases other than tremor) was significantly higher among patients with tremor ($p < 0.05$).

Our results showed that the frequency of ET among first-degree relatives was 42.1% ($n=8$), while the same rate for PT was 22.1% ($n=6$). There were no significant difference in the severity and duration of

tremor between ET cases with or without a family history ($p > 0.05$).

During the screening, neurological deficit or symptoms related to gait disturbance and ataxia could not be found in any of the patients with tremor. When concomitance of ET and PT with other movement disorders was investigated, no significant relationship was found; only one patient with concomitant PT and restless leg syndrome (RLS) was identified (Figure 1).

Table 2 summarizes clinical features of patients with ET and PT and findings during the examination. Among ET patients, the most common involvement was observed in hands ($n=19$), followed by head ($n=3$) and legs ($n=1$). PT was also most common in hands ($n=26$) followed by legs ($n=1$).

There were single instances in ET and PT groups with both hand and leg involvement, while there was one case with hand, chin, tongue, voice involvement and one case with head and hand involvement in the ET group.

When the types of tremor were examined in the ET and PT groups, postural tremor was the dominant type in both groups ($p < 0.05$). Compared to the PT group, resting tremor in the ET group was significantly more prevalent ($p < 0.05$). Symptoms were mild in both groups. A significant correlation between the duration and the severity of the tremor could not be found among ET and PT cases in different age groups. When all tremor cases were combined, the severity of tremor increased with the duration of tremor, especially between groups aged 40-49 years and those 70 years and older ($p < 0.05$).

There was a bilateral upper extremity involvement in 65% of cases with ET, while 40.7% of PT cases experienced a similar involvement. There was no significant difference between ET and PT groups in regard to symmetrical-asymmetrical involvement ($p > 0.05$). There were no sex differences in the duration of the tremor and the sites of involvement in ET and PT groups ($p > 0.05$).

Table 1. Age-specific prevalence rates of essential tremor and physiological tremor

	Age (y)	F	M	Prevalence (%)	p (intra group)	p (inter groups)
ET	40-49	0	0	0,00	-	
	50-59	7	3	6,16	$p > 0,05$	
	60-69	1	4	4,51	$p > 0,05$	
	70+	4	2	9,13	$p > 0,05$	
	TOTAL	21	12	3,34	-	
PT	40-49	4	4	2,89	$p > 0,05$	
	50-59	7	1	4,93	$p > 0,05$	
	60-69	3	3	5,41	$p > 0,05$	$p > 0,05$
	70+	3	1	6,09	$p > 0,05$	
	TOTAL	17	9	4,14	-	
TREMOR	40-49	7	4	3,97	$p > 0,05$	
	50-59	13	6	11,71	$p > 0,05$	
	60-69	5	9	12,63	$p > 0,05$	
	70+	8	4	18,26	$p > 0,05$	
	TOTAL	33	23	9,00	-	

ET: Essential tremor, PT: physiological tremor F: female, M: male

Fisher Exact Test was performed

Table 2. Clinical features of tremor

Tremor type	Essential tremor	Physiological tremor
Initial side of tremor		
Right	5 (23.8%)	12 (44.4%)
Left	3 (14.3%)	4 (14.8%)
Bilateral	13 (61.9%)	10 (40.7%)
Involvement		
Symmetrical	10 (47.6%)	10 (37%)
Asymmetrical	11 (52.4%)	16 (63%)
Duration of tremor		
<5years	3 (14.3%)	7 (25.9%)
5≤x<10years	7 (33.3%)	10 (33.3%)
≥10years	11 (52.4%)	9 (33.3%)
Localization		
Hand	19 (90.5%)	26 (100%)
Chin	1 (4.8%)	-
Leg	1 (4.8%)	1 (3.7%)
Voice	1 (4.8%)	-
Tongue	1 (4.8%)	-
Head	3 (14.3%)	-
Trunk	-	-
Type of tremor		
Resting	7 (38.4%)	2 (5.5%)
Postural	18 (47.4%)	24 (66.7%)
Kinetic	12 (31.6%)	10 (27.8%)
Task	1 (2.6%)	-
Severity of tremor		
Mild	10 (50%)	21 (81.5%)
Moderate	9 (45%)	5 (18.5%)
Severe	1 (5%)	-

DISCUSSION

In the present study, prevalence of ET was found to be 3.34%, while that of PT was 4.14%. Although there are numerous studies reporting the clinical features of ET and its worldwide prevalence, this is the second report investigating tremor prevalence in Turkey^(3-5,8,10,12,17,23,24).

In terms of methodology, with the exception of employment of video recording, the present study was similar to those of Mancini et al (Italy) and Tan et al (Singapore) with respect to the age groups and multi-phase assessment. Mancini et al calculated the prevalence rate of ET as 1.19%, while Tan et al found it to be 0.237%^(17,23). The wide range of results from the Italian and Singaporean studies suggest that race, ethnic origin, and geographical differences may contribute to prevalence rates.

Louis ED and colleagues suggested the term “mild clinically detectable normal tremor” that is correlated with increasing age in 96% of cases who were evaluated as normal previously in their population-based study⁽¹⁴⁾. We noticed that the prevalence of physiological tremor, so called “mild clinically detectable normal tremor”, was considerably lower (4.14%) in our study when compared with that study. The cause of this difference may be whether our sample size or unintentional exclusion of electrophysiological methods during the diagnosis process.

Prevalence rates of ET in the literature range between 0.005% and 22.0%, and a correlation between increased age and prevalence has been reported^(2,3). In the present study we failed to demonstrate a correlation between age and ET prevalence. Although insignificant, ET was

more frequent in the 70 years and older group. In the present study, ET was less frequent than PT. This could be related to our methodology or to our smaller sample size. The ET prevalence in the elderly population groups reported in previous studies varied considerably, from 1.3% to 23%^(2-4,10,15,16). However, reported prevalence among middle-aged and older subjects was in the range of 1.21% to 4.8% in other publications^(8,17). Collective data from the literature and the present study show that the frequency of occurrence increases with the increase in mean age of the population examined, accordingly.

The transmission of ET is autosomal dominant with variable penetrance, although some cases appear to be sporadic⁽²²⁾. In many studies, familial transmission has been reported in 50% to 70% of cases with ET. We confirmed a history of tremor in first-degree relatives of patients, but we cannot offer new data on the pattern of tremor inheritance since we were unable to follow up and run genetic tests on relatives.

Non-genetic and environmental factors have also been implicated in the etiology of ET. Among our study participants, tremor was significantly associated with beta-blockers, calcium channel blockers and oral antidiabetic drug use. This result can be attributed to the older mean age of the patients with ET (59.8 years), as well as to a significant concomitance of diabetes and hypertension among patients with ET. Therefore, it is not possible to draw a conclusion about the effect of these medications on the tremor.

A 90% upper extremity, 50% head, 30% voice, and 15% leg or chin involvement is common in ET. Mild-to-moderate asymmetric amplitude differences may be seen between affected sides^(16,22). In the present study, involvement of regions other than the upper extremity was very rare. Possible explanations could include the relatively mild rather than moderate tremor

severity, and the small number of patients with ET.

It is noteworthy that all cases of ET were diagnosed by the investigators. This shows that the awareness of ET is low, both in the society at large and among health professionals. This might either be a result of lack of knowledge among patients and physicians about movement disorders, or, since the symptoms sometimes do not affect daily activities, the patient does not necessarily consult a physician. As a result of our findings, we propose that both physicians and society at large need to be better informed about tremor.

It has been argued in the literature that RLS and ET in particular share similar pathogenesis with PD, and therefore, concomitance of these diseases was more frequent^(9,19,20). Further, concomitance of ET with gait disturbances observed in cerebellar diseases such as broad-based, ataxic, and dissymmetric gait has been reported by control tertiary centers⁽²¹⁾. In our study, there was no significant comorbidity between ET and other movement disorders and gait disorders. Previous studies on the coexistence of movement disorders were hospital-based, thus reflecting the results of the patient population of tertiary centers. In contrast, the present study is a population-based survey, and therefore it is difficult to compare our results with those of the previous studies. However, we acknowledge that the small sample size is a limitation of the present study.

Variation in the prevalence of movement disorders is generally attributed to the differences in the methodology of prevalence studies^(12,21). In the present study, participants those displayed at least one symptom indicative of tremor in phase 1 were included in phase 2 to be assessed by movement disorder specialists, and 28.1% of all participants who displayed tremor symptoms were diagnosed with tremor.

One of the major limitations of our study was small sample size. As mentioned before, there are many different prevalence rates reported from all around the world depending on the study design, genetic and geographical variabilities. We calculated our sample size regarding reports of Benito-Leon J et al, Lieberman A et al and Moghal S et al. Their ET prevalence ranges from 4,8% to 22%^(3,13,18). Therefore, we accepted the prevalence rate approximately at the level of 15%.

Consequently, the strengths of our study were the face-to-face interview method and video recordings of the subjects. Our prevalence rates fall within the wide range that has been reported in previous studies. We assume that future studies using methods similar to the present study would probably narrow the range.

Bursa and its Orhangazi District are residential areas those have rapidly growing populations because of imigration from other areas. Therefore, it is plausible to accept these regions as a representative of the demographic composition of Turkey. The prevalence rates found in the present study constitute an important data source of Turkey. In future studies, larger geographical areas and different regions with varying size and population density should be screened to contribute to the prevalence data.

Correspondence to:

Sevda Erer

E-mail: sevdaerer@uludag.edu.tr

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