

# Prevalence of essential tremor

## Door-to-door neurologic exams in Mersin Province, Turkey

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**Abstract**—Estimates of the prevalence of essential tremor (ET) are probably low because screening questionnaires have been used. The authors estimated the prevalence of ET in Mersin Province, Turkey, in 2,253 individuals aged  $\geq 40$  years, all of whom were examined by study neurologists. There were 89 ET cases (prevalence = 4.0%, 95% CI = 3.2 to 4.8%). The prevalence of ET may be higher than previously estimated. This is important when defining the extent of the health care problem.

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In most population-based prevalence studies of essential tremor (ET), screening questionnaires were used,<sup>1,2</sup> a strategy that was likely to have yielded low prevalence estimates because of the high proportion (85%) of cases who screen negative.<sup>3</sup> In other studies, participants were examined by nonneurologists,<sup>4,5</sup> which was likely to have resulted in low prevalence estimates. Therefore, current estimates of the prevalence of ET are likely to be low.

To estimate the prevalence of ET in the Mersin Province, Turkey, in individuals aged  $\geq 40$  years, all individuals were examined by a study neurologist regardless of screen results. The neurologists used a standardized examination, a tremor rating scale, and a diagnostic protocol that were developed and validated in a population-based study of ET in the United States.<sup>6</sup>

**Methods.** Mersin, an administrative province of Turkey (area = 776,000 km<sup>2</sup>), has a population of 386,777 individuals  $\geq 40$  years of age (2000 National Census); 40.3% reside in the capital city, 28.8% in other cities, and 30.9% in villages.

Based on the expected prevalence of ET (1%), a sample of 2,500 persons was selected using the Epi Info 6 program (CDC, Atlanta, GA). In the first phase, the province's 151 Primary Health Care Districts were identified and 20 districts (5 urban, 5 suburban, 10 rural) were randomly selected. Randomization was weighted according to the gender and age of the population of each district. Each ward in each district was considered a cluster. Clusters were selected randomly, and within each cluster, individuals were selected by random sampling within gender- and age-defined strata. The target study population consisted of 2,500 adults who represented 0.65% of the Mersin population  $\geq 40$  years old. At the Turkish Health Ministry (Primary Health Care Systems, Household Identification System), each household has a unique identification card. The same household was not sampled twice; if two persons in the household were eligible, the one that appeared first on the card was selected.

The epidemiologic survey used door-to-door interviews and examinations. Four study neurologists performed the evaluations; each evaluation was performed by two of the four. The neurologists visited the 2,500 residents in their homes between July and

December 2002. The researchers followed a standardized protocol for their country. As this was field work rather than work involving patients in clinics, they were required to obtain permission from the Turkish Ministry of Health. The ministry uses a board of doctors, lawyers, and ethicists to review protocols. This protocol was approved by the ministry's board prior to the start of the study. Also, all study subjects signed a consent form so that consent, in writing, was required of participants. Participants gave free and informed consent, which was maintained throughout their participation in this study.

A semistructured tremor interview was conducted,<sup>3,6</sup> including five questions to screen for ET and a question that asked whether tremor was functionally disabling. These had been translated and piloted on 60 individuals. A set of screening questions for dystonia and parkinsonism was administered. Each resident was examined using a standardized tremor examination<sup>3,6</sup> and a neurologic examination to assess signs of parkinsonism and other movement disorders. The tremor examination included 1 test for postural tremor and 5 for kinetic tremor performed with each hand (12 tests total). The two neurologists used the Washington Heights–Inwood Genetic Study of Essential Tremor tremor rating scale to rate the severity of the tremor (0 to 3) during the examination and assign a total tremor score (range = 0 to 36 [rating of 3 on 12 tests]).<sup>3,6</sup> They had been trained to use the rating scale by viewing a training tape that included educational and self-assessment sections.<sup>7</sup> The four neurologists demonstrated substantial agreement with training tape ratings (weighted  $\kappa \geq 0.70$  for each neurologist).

Based on the interview and examination, each neurologist independently assigned a diagnosis (ET or normal) using published diagnostic criteria,<sup>6</sup> which required the presence of moderate or greater amplitude kinetic tremor during three or more tests or a head tremor.<sup>6</sup> We previously demonstrated that there is excellent agreement (concordance = 94.4%,  $\kappa = 0.88$ ) between clinical diagnoses of ET based on these criteria and independent diagnoses of ET based on tremor analysis results.<sup>8</sup> A final diagnosis of ET was assigned when both neurologists agreed. When they disagreed, consensus diagnosis was reached based on review of medical information.

Analyses were performed in SPSS (version 11; Chicago, IL). In a logistic regression analysis, the risk of ET (odds ratio [OR]) was assessed as a function of age.

**Results.** Two thousand two hundred fifty-three (90.1%) of 2,500 residents participated. The 247 nonparticipants could not be found in their homes on at least two visits or

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**Table 1** Age distributions of study sample vs population of Mersin  $\geq 40$  years old

Age, y	Study sample		Mersin	
	Male, no. (%)	Female, no. (%)	Male, no. (%)	Female, no. (%)
40–49	508 (22.5)	500 (22.2)	86,465 (22.4)	82,278 (21.3)
50–59	313 (13.8)	310 (13.8)	54,893 (14.2)	53,074 (13.7)
60–69	201 (8.9)	206 (9.1)	35,669 (9.2)	35,747 (9.2)
70–79	85 (3.8)	84 (3.7)	14,701 (3.8)	15,686 (4.1)
$\geq 80$	24 (1.1)	22 (1.0)	3,706 (1.0)	4,558 (1.2)
Total	1,131 (50.2)	1,122 (49.8)	195,434 (50.5)	191,343 (49.5)

$\chi^2$  with 9 *df* = 2.96, *p* = 0.97.

refused to participate. The age and gender distributions of the study sample were similar to those of the population of Mersin  $\geq 40$  years of age (table 1). There were 89 ET cases (prevalence = 4.0%, 95% CI = 3.2 to 4.8%; table 2), of whom 74 (83.1%) answered “yes” to one or more of five screening questions for ET and 34 (38.2%) reported a family history of ET. The total tremor score was  $17.8 \pm 5.9$  (median = 16, range = 8 to 36), and 46 (51.7%) reported functional disability due to tremor. Eight (9.0%) previously had been diagnosed with ET by a physician. The prevalence was similar in men and women and increased with age. In a logistic regression model, ET was associated with age (OR = 1.03, 95% CI = 1.02 to 1.05; *p* < 0.001); the risk of ET increased by 3% with each year and by 30% with each decade.

**Discussion.** The prevalence of ET may have been underestimated in the past with screening questionnaires. In the current study, neurologists performed door-to-door examinations rather than relying on an initial screening questionnaire for case identification. The prevalence of ET was 4.0% in individuals  $\geq 40$  years. In previous population-based prevalence studies (table 3),<sup>1,2,4</sup> prevalence estimates were lower. A population-based study in Finland was similar to ours.<sup>9</sup> Those authors examined participants who screened positive to a tremor questionnaire and a

subsample who screened negative, allowing them to estimate the proportion of false negatives (21/438 = 4.8%). The prevalence of ET in individuals aged  $\geq 40$  years was 5.6% (95% CI = 4.8 to 6.4%).<sup>9</sup> In one other study in which neurologists examined all participants in a retirement community in Arizona, the prevalence of ET in individuals >65 years was 20.5% (compared with 6.7% in the current study),<sup>10</sup> but the authors did not elaborate their method of distinguishing ET from enhanced physiologic tremor, which is very common in the elderly. These data, along with our own, suggest that the prevalence of ET in individuals  $\geq 40$  years may in some populations be in the range of 4.0 to 5.6%, rather than 0.5 to 1.5%, as previously estimated based on studies that used screening questionnaires.<sup>1,4</sup>

High rates of consanguinity could yield high prevalence figures for genetic forms of ET; however, there are no cultural or religious motivations for within-family marriages in Mersin. The proportion of subjects who reported a family history of ET was similar to that in other populations.<sup>1,2</sup> Also, higher exposure to environmental factors implicated in the etiology of ET could account for the high prevalence of ET in Mersin; this should be explored.

A limitation of this study is that we restricted our

**Table 2** Crude prevalence of ET stratified by age and gender

Age stratum, y	Proportion (%) with ET: men	Proportion (%) with ET: women	Proportion (%) with ET: men and women
40–49	12/508 (2.4)	6/500 (3.2)	28/1,008 (2.8)
50–59	10/313 (3.2)	12/310 (3.9)	22/623 (3.5)
60–69	13/201 (6.5)	11/206 (5.3)	24/407 (5.9)
70–79	8/85 (9.4)	3/84 (3.6)	11/169 (6.5)
$\geq 80$	4/24 (16.7)	0/22 (0)	4/46 (8.7)
Total	47/1,131 (4.2)*	42/1,122 (3.7)†	89/2,253 (4.0)‡

For 65- to 69-y age stratum, 7 (7.6%) of 92 men and 4 (4.8%) of 83 women had ET (total = 11/175 = 6.3%). Comparisons of proportions with ET in each age stratum did not reveal any gender differences (*p* > 0.05 for all comparisons).

\* 95% CI = 1.3 to 7.1%.

† 95% CI = 0.9 to 6.5%.

‡ 95% CI = 3.2 to 4.8%.

ET = essential tremor.

**Table 3** Prevalence of ET stratified by age in population-based studies

Ref. no.	40–49 y	50–59 y	60–69 y	70–79 y	≥80 y
1	3/1,633 (0.2)		6/564 (1.1)	13/446 (2.9)	8/148 (5.4)
2*				114/2,366 (4.8)	80/1261 (6.3)
4†	27/4,643 (0.6)	65/3,894 (1.7)			
9	24/1,090 (2.2)	41/810 (5.1)	50/731 (6.8)	47/373 (12.6)	9/76 (11.8)
Current study	28/1,008 (2.8)	22/623 (3.5)	24/407 (5.9)	11/169 (6.5)	4/46 (8.7)

Values in parentheses are percentages.

\* In ref. 2, among individuals aged 65 to 69 y, 62/1,651 (3.7%) had ET.

† In ref. 4, among individuals aged ≥60 y, 79/1,921 (4.1%) had ET.

ET = essential tremor.

survey to individuals ≥40 years of age; the prevalence of ET for all ages could not be estimated. In previous epidemiologic studies, 2.2 to 3.3% of prevalent ET cases were <40 years.<sup>1,4</sup> However, all individuals were examined by a study neurologist regardless of screen results, thereby reducing the number of false-negative cases and providing a more accurate estimate of prevalence.

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