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What's Known on this subject

Tics are thought to be the most common movement disorder diagnosed in children, with a prevalence ranging from 4% to 20% of schoolchildren. However, relatively little is known about the prevalence of other tic disorders than TS, and severity of tic disorders by age groups.

What this study adds

An acceptable coverage of age range of children and adolescent population to estimate prevalence, an adequate case ascertainment strategy in different settings (mainstream schools vs. special education centers), and a description of the main attrition variables that may affect the precision in estimates.

Abstract

Background: Tic disorders are a neurodevelopmental disorder of childhood associated with psychiatric comorbidity and academic problems. The purpose of this project is to determine the prevalence of tic disorders in a school-based study.

Method: Cross-sectional study. A randomized sample of 1,158 schoolchildren based on clusters (classrooms) in the province of Burgos (Spain), was identified on a stratified sampling frame constituted by strata combining type of educational center (state-assisted, public, urban or suburban) and type of education (mainstream schools and special education), using a two phase approach (screening and diagnosis ascertainment by a neurologist). Tics were diagnosed based on DSM-IV TR criteria (with/without impairment criterion).

Results: In mainstream schools, tics were found in 125/741 subjects (16.86%, 95 % CI 14.10-19.63, adjusted prevalence to the standard European population of 16.60%), and were more frequent in males [87/448 (19.42%, 95% CI 15.64-23.19, adjusted prevalence 18.43%)], compared to females [38/293 (12.96%), 95% CI 8.95-16.98, adjusted prevalence 13.45%, p=0.03]. In special education centers, tics disorders were found in 11/54 of children (20.37%, 95% CI: 8.70-32.03). Overall, tics with impairment criterion were less frequent than tics without impairment criterion (adjusted prevalence estimates of 4.65% vs. 11.85%, p<0.0001), and were more frequent in males compared to females (p= 0.03). The most frequent tic diagnoses were chronic motor tics (6.07%, 95% CI:4.28-7.86) and Tourette syndrome (5.26%, 95% CI:3.58-6.93).

Conclusion: Tic disorders are common in childhood. Based on the diagnostic criteria, the use or not of impairment criterion has a significant impact on tic prevalence estimates.

Introduction

Tic disorders are a hereditary neurodevelopmental disorder of childhood characterized by being sudden, repetitive, stereotyped motor movements or sounds, with a longitudinal outcome of gradual improvement in most subjects.[1] Several widely used diagnostic classifications for tic disorders include the diagnostic and Statistical Manual of Mental disorders, [2] the International Classification of disease and Related Health Problems 10th revision,[3] and the Classification of Tic disorders developed by the Tourette Syndrome Classification Study Group. [4] Although clear differences exist between these classification schemes, they are broadly congruent, with each containing well specified categories; 1) Tourette Syndrome (TS), 2) chronic motor or vocal tic disorder (CMT, CVT), 3) Transient tic disorder (TTD), and 4) non specified tic disorders (NSTD).

Knowledge of the prevalence of different tic disorders is critical for planning and early support in education and health care, due to the important association of tic disorders with psychiatric conditions and academic difficulties. [5] However, the epidemiology of tic disorders are more complex than was previously thought. Until fairly recently, tic disorders were considered to be rare,[6] but today tics are thought to be the most common movement disorder diagnosed in children, with 4% to 20% of schoolchildren experiencing tics during their lifetime.[7-17] Tentative explanations for differing prevalence estimates include the multidimensional nature of tics, and the use of different epidemiological methods. [8, 18] However, up to date, relatively little is known about the prevalence of tic disorders other than TS, and severity of tic disorders by age groups.[13-17] Likewise, few studies have reported detailed information about the prevalence of tic disorders in different settings such as special education centers. [19-21]

The purpose of this project was first to determine the prevalence of tic disorders with and without impairment and by age-groups using a school-based epidemiological study from mainstream schools and special education centers; and second to describe the main attrition variables in this type of cohort.

Methods

2.1 Setting, design, sample and procedures

This study was conducted between March 2007 and December 2009, in the Neurology Department (Hospital General Yagüe, Burgos, Spain), and is part of a cross-sectional study aimed at studying the prevalence of tic disorders and their association with academic difficulties. A prior pilot study was first conducted in 2007-2008, in 2 schools to validate our screening procedures compared to the gold standard (neurological diagnosis established by the neurologist).[22] Participants were students aged 6 to 16 years from mainstream schools and special education centers, in the province of Burgos, Spain. In 2007, the total number of students from 6 to 16 years old was 28,706. Before starting this project, we received a computerized roster from the school district of all students using unique confidential identification codes along with each student's gender, age, school, educational placement (urban/suburban), school financial support (public/state assisted), and academic characteristics (grades and current need to repeat a grade). We used a stratified sampling plan with three stratification variables: educational placement (urban defined as school placed in city with more than 30,000 inhabitants versus suburban), financial support (100 % public vs. state assisted), and level (elementary, middle and high school). We calculated that a cohort of nearly 1,100 students including mainstream schools and special education centers, was necessary according to the prevalence rate of tic disorders (assuming the rarest estimate of 4%), with 95% confidence intervals, and estimating a 15%

withdrawal. Mainstream schools were therefore randomly selected (random digit table, Epidata software version 3.1) and 4 mainstream schools finally agreed to participate (2 urban [50%], and 2 suburban schools [50%], 3 out of 4 were state assisted schools [75%], and 1 public school [25%]). All of them (100%) included from first grade to sixth grade, and 2 schools [50%] were middle and high schools. Owing to the small eligible sample from special education centers (111 subjects), all centers in the province of Burgos (5 special education centers) were invited to participate.

This study was carried out in 2 phases. *Phase 1* involved the application of the screening tool, and *phase 2* the ascertainment of tic diagnosis, and type of tic disorders, performed by the neurologist, who interviewed by telephone, the parents of all participants with possible tics and matched possible unaffected subjects in terms of age, gender, and classroom.

2.2 Data collection

2.2.1 Screening tools

We developed a two-stage screening tool to be used in this study. First, a Proxy-Report Questionnaire (PRQ) [23] was completed by parents and teachers, and second, the subjects were observed by trained lay observers (one psychologist [SS], and two school teachers [VA, VD]). Our procedures for the selection of subjects and the assessment of tics were previously described. [22] In mainstream schools, the sensitivity of the field study screening battery for tic disorders compared to the gold standard (neurological diagnosis established by the neurologist) was 99/125 (79%, 95% CI, 71.68-86.70), specificity of 147/176 (98%, 95% CI, 94.26-99.58), positive predictive value (PPV) of 99/102 (97%, 95% CI, 91.64-99.38), and the negative predictive value (NPV) of 147/176 (98%, 95% CI, 94.30-99.58). In special education centers, the sensitivity of the

screening battery was 8/11 (73%, 95% CI 39.02-93.97), specificity of 15/26 (58%, 95% CI 36.77-78.60), PPV of 8/19 (42%, 95% CI 20.25.66.50), NPV of 15/18 (83%, 95% CI 58.58-96.42).

2.2.3 Ascertainment of diagnosis

The clinical diagnosis of tic disorders was considered as the gold standard and it was performed by one movement disorders neurologist (EC) to reduce variability. Our procedures for the ascertainment of diagnosis were previously described. [22] Briefly, to formulate a diagnosis of tic based on history, a telephone semi-structured interview with one of the parents was used. Therefore, if all essential criteria for tics were fulfilled, a diagnosis of tic by history was reached. Instead, if some of the essential criteria were not fulfilled a diagnosis of possible tic was reached. Unaffected matched subjects in terms of age, gender and classroom, were also ascertained by the neurologist. In special education centers, due to the complexity of the phenomenology of the repetitive motor and vocal behaviors, the neurologist [EC] also observed the classroom for 1 hour, and therefore ascertainment of diagnosis was based on neurologist observation, and parent telephone interview.

The clinical diagnosis of tic disorders and type, were established if the participant had tics based on telephone semi-structured interview with the parent, by using the DSM-IV TR criteria with/without impairment criterion.[2] Tic severity and impairment was assessed by neurologist using the Yale Global Tic Severity Scale (YGTSS).[24,25] Based on the YGTSS, impairment was reported when tics were associated with associated with any difficulties in self-esteem, family life, social acceptance, or school or job functioning. [24] Tic disorders were then classified as TS, CMT, CVT, TTD, and NSTD.

2.3 Ethical Issues

The study protocol was approved by the ethical review board of the Burgos Hospital Complex Ethics Committee and School government district (Consejeria de Educación de Castilla y León), and the local school authorities, acting as the ethical committee for each school. Written consent from a parent/guardian was requested and if the parent declined to participate in the study, no data were collected on that child.

2.4 Data analysis

Statistical analyses all cross-sectional, were performed using SPSS Version 17.0 (SPSS, Inc., Chicago, IL). All tests were two-sided using a level of significance (alpha = 0.05). Descriptive statistics [i.e. means ± standard deviations, range and 95% confidence intervals (CI) based on the Poisson distribution], were used to describe the demographic and clinical data. Mann-Whitney and Chi-square tests, were used for comparisons, as appropriate. No adjustments were performed for multiple test comparisons. The prevalence rates were estimated as the number of cases per 100 people in December 2009. For prevalence rates we only used data from definitive tics. We obtained the age- and sex-specific prevalence of tic disorders with and without impairment criterion, and tic diagnosis in mainstream schools. The prevalence tables are presented in age groups. Prevalence rates obtained from mainstream schools were adjusted to the Standard European Population, so the estimates reflected the demographic distribution of European children and adolescents. [26] In special education centers, due to the low sample, overall prevalence of different tic disorders, with and without impairment criterion, was analyzed.

Results

Subjects. At the beginning of the field study, in September of 2008, letters explaining the need of the survey due to the lack of information about the frequency of tics in

Spain and inviting participation, were mailed to 1,047 parents out of 28,706 eligible participants from mainstream schoolchildren in the province of Burgos (Figure 1), and 111 parents from special education centers. In *phase 1,* at least one screening survey was completed in 741 scholars from mainstream schools, 445 (60%) males, 296 (40%) females with a mean age of 10.98 ± 2.98 years. In *phase 2*, 334 subjects (179 without tics, and 145 subjects with possible tics), out of 390 eligible subjects (195 subjects with possible tics and 195 controls), were interviewed by the neurologist (EC) for clinical ascertainment of tics (Table 1). Compared to assessed patients with tics, the non-assessed group of participants was similar to the enrolled group in terms of gender (Chi square test, p=0.14), age (Mann-Whitney test, p=0.48), parent working status (both parents working, Chi-square test, p=0.21), home distance to school location (Chi-square test, p values ranging from 0.40-0.65), and school location (urban vs. suburban, Chi-square test, p=0.60). On the other hand, the proportion of younger and Caucasian participants with academic failure in the enrolled group was higher compared to non-participants (Chi-square tests, p<0.0001, p=0.03, p< 0.0001, respectively). In special education centers, 54 out of 111 subjects were included (51%), 38 males (70%) and 16 females (30%). Compared to non participants, there was no statistical difference in terms of age (11.49 ± 3.98 years vs. 10.40 ± 3.20 years, Mann-Whitney test, p=0.46), but there was a trend towards having more males participants compared to females (57% vs. 37%, Chi-square test, p=0.05).

Prevalence of tics

Mainstream schools: Based on the neurologist ascertainment, tics were found in 125/741 subjects (16.86%, 95 % CI 14.10-19.63), adjusted prevalence of 16.60%. Tics were more frequent in males [87/448 (19.42%), 95% CI [15.64-23.19], adjusted prevalence 18,43%, compared to females [38/293 (12.96%), 95% CI 8.95-16.98],

adjusted prevalence 13.45%, Chi-square test, p=0.03), with a ratio male/female of 2.28. Instead possible tics were found in 65/334 participants (19.46%, 95% CI 15.06-23.85), with a higher frequency of males compared to females (73% males vs. 30% females, Chi-square test, p=0.02). Tics with impairment criterion was more frequent in males compared to females (25 males [86.2%] vs. 4 females [13.8%], Chi-square test, p=0.03). Among the population of students currently repeating a grade, the proportion of participants with tics was similar compared with non repeaters [8 (6.3%) vs. 11 (7.4%), Chi-square test, p=0.81]. The crude prevalence of any tic disorders was similar throughout different age groups, with a slight decrease in the oldest age group (Table 2). In contrast, tics with impairment criterion were more frequent in the oldest group. Tic severity was clearly higher among those subjects with impairment criterion compared to those without impairment criterion (YGTSS mean score of 40.52 $\pm$ 16.40 vs. 13.28 $\pm$ 9.77, Mann-Whitney test, $p< 0.0001$), but was similar between males and females (Mann-Whitney test, p=0.65). Among tic disorders, CMT and TS were the most frequent tic diagnosis. Our results for tic syndromic diagnosis are summarized in Tables 3, 4. Of the 125 participants identified with tics, in 71 (57%), tics were previously recognized by parents.

Special education centers: The neurologists assigned any tic disorders to 11/54 of children in the special education centers (20.37%, 95% CI: 8.70-32.03), and 14 with possible tic disorders (25.92%, 95% CI 13.31-38.54). Among those subjects with definitive tic disorders, 7 subjects were diagnosed with TS (2 with impairment criterion, 3.70%, 95% CI 0.45-12.74, and 5 without impairment criterion, 9.25%, 95% CI 3.07-20.30), 2 with CMT tics without impairment criterion (3.70%, 95% CI 0.45-12.74, and 2 with NSTD (3.70%, 95% CI 0.45-12.74). There were no differences in the frequency of tics in terms of gender (males 7/11 (63%) vs. females 4/11 (37%), Chi-square test,

p=0.58). According to the neurologist observation, other repetitive motor behaviors such as stereotypes, and unclassified repetitive motor and vocal behaviors were observed in 17 subjects [31.48% (95% CI 18.16-44.79)], respectively. Overall, out of 9 subjects diagnosed with autism spectrum disorders, tics were found in 3 subjects (33.33%, 95% CI 7.48-70.07), 5 out of 23 subjects diagnosed with chromosomal disease (Down syndrome) (21.73%, 95% CI 7.46-43.70) and 3 out of 14 subjects diagnosed with intellectual disability of unknown etiology (33.33%, 95% CI 7.48-70.07).

Discussion

To our knowledge, this is one of the most detailed school-children based sample of prevalence of tic disorders conducted in mainstream schoolchildren and special education centers. Specific strengths of this study include: 1) an acceptable coverage of age range of children and adolescent population to estimate prevalence; 2) an adequate prior validation of screening battery in different settings (mainstream schools vs. special education centers), 3) a description of the main attrition variables that may affect the precision in estimates, and 4) detailed information about the prevalence of different tic disorders analyzing the impact of impairment criterion. Important new findings demonstrate that disability associated with tics seems to be greater in males compared to females, and in older adolescents, or at least this is how it is observed by their parents. Gender and aging issues about coping tics, and how associated comorbidities may impact on tic disability in males, require clarification in further studies. Tic phenomenology seems to vary with age, with a lower frequency of vocal tics in late adolescence most likely due to suppression, or because they spontaneously disappeared, especially in females, in contrast to other studies, where no significant differences in tic phenomenology were seen. [27] However, a bias due to the small sample of adolescents included, make the extrapolation of our results to the general population controversial.

Our study has identified similar adjusted prevalence estimates of 16.60% for any tic disorder, compared to previously reported prevalence estimates in mainstream schools, [10,11,16,19] but higher than the 6.5% prevalence estimate observed in two selected schools in Spain. [23] In agreement with other studies, [19,28] we found that impairment criterion significantly impacts the prevalence of tic disorders, and it may explain, at least partially, the wide range of prevalence estimates previously reported. Among tic disorders, CMT and TS, were the most frequent tics diagnosis, in accordance with other epidemiological studies. [19,28] Likewise, we also found that the prevalence of tic disorders was higher in the youngest group of 5 to 9 years, [16] particularly in girls, most likely due to a higher presence of transient tic and NSTD. In contrast, chronic tics seem to be more frequent in males compared to females, but in order to confirm this hypothesis longitudinal studies are further required.

In agreement with other authors, we found a higher prevalence of chronic tic disorders in the special education sample compared to the mainstream sample.[19-21] Among those subjects with mental disability, tics were especially frequent in subjects with Autism Spectrum Disorders, [29] and surprisingly in Down syndrome as well.[30] However, the extrapolation of our results can be limited, due the high complexity of diagnosing tics in this population, and the small sample size.

In order to compare our results with other epidemiological studies in tic disorders, we need to discuss the main methodological issues for epidemiological surveys. Overall, the three most important methodological elements are: 1) the case ascertainment strategy, 2) the definition of tic disorders, and 3) the degree of coverage of the eligible population (response rate). First, the screening methodology applied in this study was previously validated and sensitive to detect subjects with tics. In this regards, few studies have previously reported the sensitivity of their screening

procedures. [15,16,19] Likewise, classically the diagnosis of tic disorders is either ascertained by trained technicians,[19] is performed in positively screened subjects only, [15, 16] or the level of certainty of diagnosis is unknown. In our study, ascertainment was performed by one movement disorders neurologist by using a telephone-based interview which showed an excellent intra-rater reliability (*kappa coefficient* of 0.83), compared to face to face interviews.[23] All possible cases and matched possible unaffected cases were ascertained to decrease the number of false negative and false positive cases, and the level of certainty was obtained. A potential advantage of using this type of ascertainment is that telephone interviews could decrease the burden of face-to face interviews, thereby increasing the participation of patients and their relatives, making it easier to perform epidemiological surveys. But, on the other hand, a high number of possible cases with tics was found, and may limit the precision of our estimates. Likewise, the application of different clinical criteria for tic diagnosis and the use of impairment criterion significantly influence prevalence estimates and it may be risky to compare surveys that have used them differently. Third, overall we had a good response rate in mainstream schools (70% of the original sample in the screening phase), higher than in other studies, [19] and 84% in the ascertainment phase, but low in the special education centers (49% in the screening and ascertainment phase). A detailed description and analysis of attrition variables is of major importance to analyze the precision of frequency estimates and for future epidemiological studies to enroll participants at higher risk of dropout. Since we do not have data on non-responders for the first stage of attrition (screening phase), we found that non Caucasians adolescent participants, without academic problems, are at higher risk of dropout in mainstream school samples.

This study has several limitations, including a possible selection bias with small sample size in certain age groups, higher proportion of male participants compared to females, and lack of information on other age groups such as adults. In this regards, adult-onset tic disorders have been documented, but they often had different etiologies.[31,32] We may also have underestimated the prevalence of tics that were transient and not present at the time due to recall bias. Conversely, we might have over-diagnosed children with tics due to the excessive diagnostic enthusiasm of parents, teachers and clinicians, leading to the inclusion of children with a dubious diagnosis.

In closing, tic disorders are common in a childhood population. The use of impairment criterion significantly impact on the tic prevalence estimates. The appeal of using the impairment criterion as a means of distinguishing cases from non- cases of tic disorders is also controversial, because we cannot clearly establish the source of impairment (tics vs. associated comorbidities).[33] Because tics and higher disability are more frequent in males compared to females and in adolescents, gender and aging issues about tic-related disability require clarification in further studies.

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References

1. Abell S, Ey J. Tics in childhood. Clin Pediatr (Phila) 2009;48:790-791.

2. Association. AP, ed. Diagnostic and statistical manual of mental disorders (4th ed.-Text revision) ed. Washington DC: American Psychiatric Association; 2000.

3. International Statistical Classification of Diseases and Related Health Problems, 10th Ed. Geneva WHO; 1992.

4. Definitions and classification of tic disorders. The Tourette Syndrome Classification Study Group. Arch Neurol 1993;50:1013-1016.

5. Singer HS, Schuerholz LJ, Denckla MB. Learning difficulties in children with Tourette syndrome. J Child Neurol 1995;10 Suppl 1:S58-61.

6. Robertson MM. Diagnosing Tourette syndrome: is it a common disorder? J Psychosom Res 2003;55:3-6.

7. Comings DE, Himes JA, Comings BG. An epidemiologic study of Tourette's syndrome in a single school district. J Clin Psychiatry 1990;51:463-469.

8. Robertson MM. The prevalence and epidemiology of Gilles de la Tourette syndrome. Part 2: tentative explanations for differing prevalence figures in GTS, including the possible effects of psychopathology, aetiology, cultural differences, and differing phenotypes. J Psychosom Res 2008;65:473-486.

9. Nomoto F, Machiyama Y. An epidemiological study of tics. Jpn J Psychiatry Neurol 1990;44:649-655.

10. Hornsey H, Banerjee S, Zeitlin H, Robertson M. The prevalence of Tourette syndrome in 13-14-year-olds in mainstream schools. J Child Psychol Psychiatry 2001;42:1035-1039.

11. Snider LA, Seligman LD, Ketchen BR, et al. Tics and problem behaviors in schoolchildren: prevalence, characterization, and associations. Pediatrics 2002;110:331-336.

12. Gadow KD, Nolan EE, Sprafkin J, Schwartz J. Tics and psychiatric comorbidity in children and adolescents. Dev Med Child Neurol 2002;44:330-338.

13. Wang HS, Kuo MF. Tourette's syndrome in Taiwan: an epidemiological study of tic disorders in an elementary school at Taipei County. Brain Dev 2003;25 Suppl 1:S29-31.

14. Jin R, Zheng RY, Huang WW, et al. Epidemiological survey of Tourette syndrome in children and adolescents in Wenzhou of P.R. China. Eur J Epidemiol 2005;20:925-927.

15. Lanzi G, Zambrino CA, Termine C, et al. Prevalence of tic disorders among primary school students in the city of Pavia, Italy. Arch Dis Child 2004;89:45-47.

16. Khalifa N, von Knorring AL. Prevalence of tic disorders and Tourette syndrome in a Swedish school population. Dev Med Child Neurol 2003;45:315-319.

17. Stefanoff P, Mazurek J. Epidemiological methods used in studies in the prevalence of Tourette syndrome. Psychiatr Pol 2003;37:97-107.

18. Robertson MM. The prevalence and epidemiology of Gilles de la Tourette syndrome. Part 1: the epidemiological and prevalence studies. J Psychosom Res 2008;65:461-472.

19. Kurlan R, McDermott MP, Deeley C, et al. Prevalence of tics in schoolchildren and association with placement in special education. Neurology 2001;57:1383-1388.

20. Kurlan R. Tourette syndrome in a special education population. Hypotheses. Adv Neurol 1992;58:75-81.

21. Eapen V, Robertson MM, Zeitlin H, Kurlan R. Gilles de la Tourette's syndrome in special education schools: a United Kingdom study. J Neurol 1997;244:378-382.

22. Cubo E, Saez S, Delgado Benito V, Ausín Villaverde V, et al. Validation of screening instruments for neuroepidemiological surveys of tic disorders. Mov Disord (In press 2010).

23. Linazasoro G, Van Blercom N, de Zarate CO. Prevalence of tic disorder in two schools in the Basque country: Results and methodological caveats. Mov Disord 2006;21:2106-2109.

24. Leckman JF, Riddle MA, Hardin MT, et al. The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. J Am Acad Child Adolesc Psychiatry 1989;28:566-573.

25. Garcia-Lopez R, Perea-Milla E, Romero-Gonzalez J, et al. Spanish adaptation and diagnostic validity of the Yale Global Tics Severity Scale. Rev Neurol 2008;46:261-266.

26. Waterhouse, J.,Muir, C.S.,Correa, P.,Powell, J., eds. Cancer Incidence in Five Continents, Vol. III IARC Scientific Publications No. 15, Lyon, IARC; 1976.

27 . Cubo E, Chmura T, Goetz CG. Comparison of tic characteristics between children and adults. Mov Disord 2008;23:2407-2411.

28. Mason A, Banerjee S, Eapen V, Zeitlin H, Robertson MM. The prevalence of Tourette syndrome in a mainstream school population. Dev Med Child Neurol 1998;40:292-296.

29. Canitano R, Vivanti G. Tics and Tourette syndrome in autism spectrum disorders. Autism 2007;11:19-28.

30. Barabas G, Wardell B, Sapiro M, Matthews WS. Coincident Down's and Tourette syndromes: three case reports. J Child Neurol 1986;1:358-360.

31. Chouinard S, Ford B. Adult onset tic disorders. J Neurol Neurosurg Psychiatry 2000;68:738-743.

32. Eapen V, Lees AJ, Lakke JP, Trimble MR, Robertson MM. Adult-onset tic disorders. Mov Disord 2002;17:735-740.

33. Scahill L, Tanner C, Dure L. The epidemiology of tics and Tourette syndrome in children and adolescents. Adv Neurol 2001;85:261-271.

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1. Research project: A. Conception, B. Organization, C. Execution;
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
3. Manuscript: A. Writing of the first draft, B. Review and Critique;

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Figure 1 Flow chart of eligible, screened and examined participants

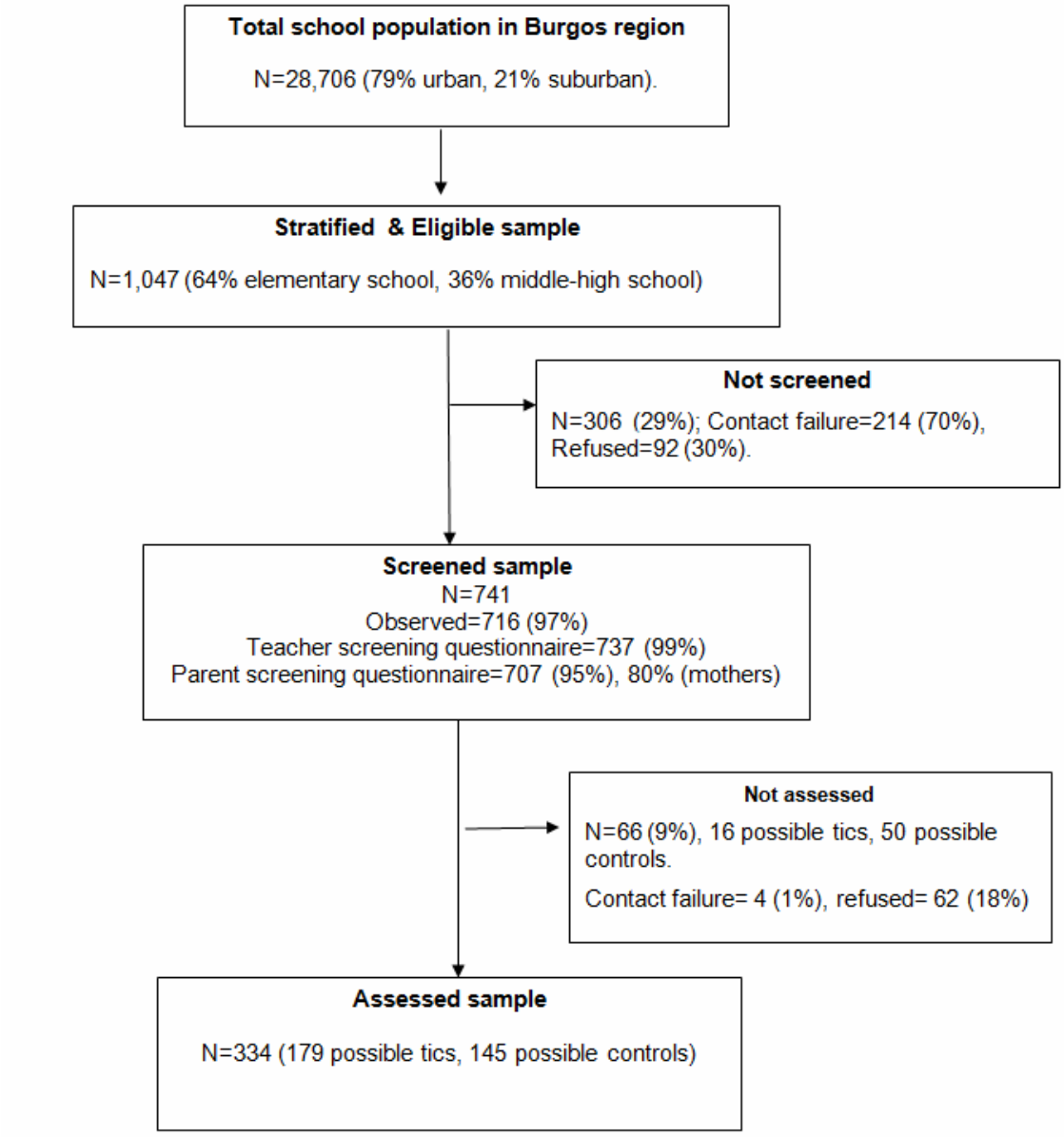

Table 1 Demographic and clinical characteristics of patients with tics

	Mainstream schools N=125	**Special education centers N=54**
Age (years old)		
Mean (SD)	10.90 (2.85)	11.40 (3.30)
Median (Range)	10 (5-17)	11 (5-17)
Gender		
Male (%)	87 (70)	32 (60)
Race		
Non Caucasian (%)	6 (5)	9 (17)
Urban school location (%)	82 (65)	54(100)
Elementary School (%)	93 (47)	-
Intellectual disability etiology (%)		
Unknown	-	14 (25)
Chromosomal Diseases (Down synd.)	-	23 (42)
Malformations	-	3 (5)
Cerebral palsy	-	5 (8)
Autism Spectrum disorders	-	9 (15)
Intellectual disability severity (%)		
Mild	-	7 (12)
Moderate	-	35 (66)
Severe	-	12 (23)

Cubo 2

Table 2. Age-and sex-specific prevalence (per 100 population) of tic disorders with/without impairment criterion in mainstream schools

Age group	Girls	Boys	Both
Any tic disorder			
6-9 years			
N. of cases (population size)	22 (113)	25 (151)	47(264)
Prevalence (95% CI)	19.4 [11.72-7.21]	16.5 [10.29-22.80]	17.8 [12.99-22.60]
Adjusted prevalence	6.48	5.51	5.93
10-14 years			
N. of cases (population size)	11 (142)	51 (231)	62(373)
Prevalence (95% CI)	7.7 [2.99-12.49]	22 [16.5127.64]	16.5[12.71-20.53]
Adjusted prevalence	2.58	7.35	5.54
15-17 years			
N. of cases (population size)	5 (38)	11 (66)	16 (104)
Prevalence (95% CI)	13.15 [4.41-28.08]	16.66 [6.91-26.41]	15.38 [7.97-22.80]
Adjusted prevalence	3.50	5.05	4.48
Any age (6-17 years)			
N. of cases (population size)	38 (293)	87 (448)	125 (741)
Prevalence (95% CI)	12.96 [8.95-16.98]	19.42 [15.64-23.19]	16.86 [14.10-19.63]
Adjusted prevalence	13.45	18.43	16.60
Tics with impairment criterion			
6-9 years			
N. of cases (population size)	2 (113)	4 (151)	6 (264)
Prevalence (95% CI)	1.7 [0.21-6.24]	2.6 [0.72-6.64]	2.2 [0.28-4.26]
Adjusted prevalence	0.58	0.88	0.75
10-14 years			
N. of cases (population size)	0 (142)	16 (231)	16 (373)
Prevalence (95% CI)	(0)[0-2.56]	6.92 [3.43-10.41]	4 [1.89-6.14]
Adjusted prevalence	0	2.30	1.42
15-17 years			
N. of cases (population size)	2 (38)	5 (66)	7 (104)
Prevalence (95% CI)	5.2 [0.64-17.74]	7.57 [2.50-16.80]	5.7 [0.80-10.73]
Adjusted prevalence	1.75	2.52	2.24
Any age (5-17 years)			
N. of cases (population size)	4 (293)	25 (448)	29 (741)
Prevalence (95% CI)	1.36 [0.37-3.45]	5.13 [2.97-7.28]	3.91 [2.45-5.37]
Adjusted prevalence	2.23	5.71	4.43
Tics without impairment criterion			
6-9 years			
N. of cases (population size)	20 (113)	21 (151)	41 (264)
Prevalence (95% CI)	17.6 [10.22-25.17]	13.9) [8.05-19.75]	15.5 [10.97-20.08]
Adjusted prevalence	5.89	4.63	5.17
10-14 years			
N. of cases (population size)	11 (142)	35(231)	46 (373)
Prevalence (95% CI)	7.7 [2.99-12.49]	15.1 [10.31-19.99]	12.3 [8.86-15.80]
Adjusted prevalence	2.58	5.05	4.11
15-17 years			
N. of cases (population size)	2 (38)	6 (66)	8 (104)
Prevalence (95% CI)	5.2 [0.64-17.74]	9 [1.39-16.78]	7.6 [2.09-13.29]
Adjusted prevalence	1.75	3.03	2.56
Any age (5-17 years)			
N. of cases (population size)	33 (293)	62 (448)	95 (741)
Prevalence (95% CI)	11.26 [7.47-15.05]	13.83 [10.53-17.14]	12.82 [10.34-15.29]
Adjusted prevalence	10.23	12.71	11.85

Table 3. Age-and sex-specific prevalence (per 100 population) of tic diagnosis with impairment criterion in mainstream schools

	Girls	Boys	Both
Tourette syndrome			
6-9 years			
N. of cases (population size)	1 (113)	2 (151)	3 (264)
Prevalence (95% CI)	0.8 [0-4.8]	1.3[0.1-4.7]	1.1 [0.2-3.2]
Adjusted prevalence	0.29	0.44	1.2 0.37
10-14 years			
N. of cases (population size)	0 (142)	6 (231)	6 (373)
Prevalence (95% CI)	0 [0-2.5]	2.59 [0.33-4.86]	1.60 [0.19-3.01]
Adjusted prevalence	0	0.86	0.35
15-17 years			
N. of cases (population size)	1 (38)	2 (66)	3 (104)
Prevalence (95% CI)	2.6 [0-13.8]	3 [0.3-10.5]	2.8 [0.5-8.1]
Adjusted prevalence	0.87	1.01	0.96
Any age (5-17 years)			
N. of cases (population size)	2 (293)	10 (448)	12 (741)
Prevalence (95% CI)	0.68 [0.08-3.45]	2.23 [0.75-3.71]	1.61 [0.64-2.59]
Adjusted prevalence	1.11	2.31	1.87
Chronic motor tic disorder			
6-9 years			
N. of cases (population size)	0 (113)	0 (151)	0 (264)
Prevalence (95% CI)	0 [0-3.2]	0 [0-2.4]	0 [0-1.3]
Adjusted prevalence	0	0	0
10-14 years			
N. of cases (population size)	0 (142)	6 (231)	6 (373)
Prevalence (95% CI)	0 [0-2.5]	2.5[0.3-4.8]	1.6 [0.1-3]
Adjusted prevalence	0	0.86	0.53
15-17 years			
N. of cases (population size)	1 (38)	1 (66)	2 (104)
Prevalence (95% CI)	2.6 [0-13.8]	1.5 [0-8.1]	1.9 [0.2-6.7]
Adjusted prevalence	0.87	0.50	0.64
Any age (5-17 years)			
N. of cases (population size)	1 (293)	7 (448)	8 (741)
Prevalence (95% CI)	0.34 [0.00-1.88]	1.56 [0.30-2.82]	1.08 [0.26-1.89]
Adjusted prevalence	0.87	1.37	1.17
Chronic vocal tic disorder			
6-9 years			
N. of cases (population size)	0 (113)	1 (151)	1 (264)
Prevalence (95% CI)	0 [0-3.2]	0.6 [0-3.6]	0.3 [0-2.7]
Adjusted prevalence	0	0.22	0.12
10-14 years			
N. of cases (population size)	0 (142)	1 (231)	1 (373)
Prevalence (95% CI)	0 [0-2.5]	0.4 [0-2.3]	(0.2 [0-1.4]
Adjusted prevalence	0	0.14	0.08
15-17 years			
N. of cases (population size)	0 (38)	0 (66)	0 (104)
Prevalence (95% CI)	0 [0-9.2]	0 [0-5.4]	0 [0-3.4]
Adjusted prevalence	0	0	0
Any age (5-17 years)			
N. of cases (population size)	0 (293)	2 (448)	2 (741)
Prevalence (95% CI)	0 [0.37-3.45]	0.44 [0.05-1.60]	0.27 [0.03-0.97]
Adjusted prevalence	0	0.36	0.21
Transient tic disorder			
6-9 years			
N. of cases (population size)	1 (113)	1 (151)	2 (264)
Prevalence (95% CI)	0.8 [0-4.8]	0.6 [0-3.6]	0.7 [0-2.7]

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Adjusted prevalence	0.29	0.22	0.25
10-14 years			
N. of cases (population size)	0 (142)	1 (231)	1 (373)
Prevalence (95% CI)	0 [0-2.5]	0.6 [0.1-1.4]	0.2 [0-1.4]
Adjusted prevalence	0	0.14	0.08
15-17 years			
N. of cases (population size)	0 (38)	1 (66)	1 (104)
Prevalence (95% CI)	0 [0-9.2]	1.5 [0-8.1]	0.9 [0-5.2]
Adjusted prevalence	0	0.50	0.32
Any age (5-17 years)			
N. of cases (population size)	1 (293)	3 (448)	4 (741)
Prevalence (95% CI)	0.34 [0.00-1.88]	0.67 [0.13-1.94]	0.54 [0.14-1.37]
Adjusted prevalence	0.29	0.87	0.66
Non-specified tic disorder			
6-9 years			
N. of cases (population size)	0 (113)	0 (151)	0 (264)
Prevalence (95% CI)	0 [0-3.2]	0 [0-2.4]	0 [0-1.3]
Adjusted prevalence	0	0	0
10-14 years			
N. of cases (population size)	1 (142)	1 (231)	2 (373)
Prevalence (95% CI)	0.7 [0-3.8]	0.6 [0.1-1.4]	0.5 [0-1.9]
Adjusted prevalence	0.23	0.14	0.17
15-17 years			
N. of cases (population size)	1 (38)	0 (66)	1 (104)
Prevalence (95% CI)	2.6 [0-13.8]	0[0-5.4]	0.9 [0-5.2]
Adjusted prevalence	0.87	0	0.32
Any age (5-17 years)			
N. of cases (population size)	2 (293)	1 (448)	3 (741)
Prevalence (95% CI)	0.34 [0.00-1.23]	0.22 [0.00-1.23]	0.40 [0.08-1.17]
Adjusted prevalence	1.11	0.14	0.49

Table 4. Age-and sex-specific prevalence (per 100 population) of tic diagnosis without impairment criterion in mainstream schools

	Girls	Boys	Both
Tourette syndrome			
6-9 years			
N. of cases (population size)	7 (113)	5 (151)	13 (264)
Prevalence (95% CI)	6.19 [1.30-11.08]	3.1 [1.58-7.55]	4.9 [2.12-7.72]
Adjusted prevalence	1.67	1.10	1.64
10-14 years			
N. of cases (population size)	5 (142)	7 (231)	12 (373)
Prevalence (95% CI)	3.5 [1.1-8]	3.03[0.6-5.4]	3.2 [1.29-5.14]
Adjusted prevalence	1.17	1.01	1.07
15-17 years			
N. of cases (population size)	0 (38)	3 (66)	3 (104)
Prevalence (95% CI)	0 [0-9.2]	4.5 [0.9-12.7]	2.8 [0.5-8.1]
Adjusted prevalence	0	1.51	0.96
Any age (5-17 years)			
N. of cases (population size)	12 (293)	15 (448)	27 (741)
Prevalence (95% CI)	4.09 [1.65-6.53]	3.34 [1.57-5.12]	3.64 [2.22-5.06]
Adjusted prevalence	2.85	3.62	3.67
Chronic motor tic disorder			
6-9 years			
N. of cases (population size)	5 (113)	9 (151)	14 (264)
Prevalence (95% CI)	4.4 [1.45-10.02]	5.9 [1.85-10.06]	5.3 [2.41-8.19]
Adjusted prevalence	1.47	1.98	1.76
10-14 years			
N. of cases (population size)	4 (142)	15 (231)	19 (373)
Prevalence (95% CI)	2.8 [0.7-7]	6.4[3-9.8]	5.09 [2.72-7.45]
Adjusted prevalence	0.93	2.16	1.69
15-17 years			
N. of cases (population size)	1 (38)	3 (66)	4 (104)
Prevalence (95% CI)	2.6 [0-13.8]	4.5 [0.9-12.7]	3.8 [1-9.5]
Adjusted prevalence	0.87	1.51	1.28
Any age (5-17 years)			
N. of cases (population size)	10 (293)	27 (448)	37 (741)
Prevalence (95% CI)	3.41 [1.16-5.66]	3.64 [2.22-5.06]	4.99 [3.35-6.60]
Adjusted prevalence	3.29	5.66	4.74
Chronic vocal tic disorder			
6-9 years			
N. of cases (population size)	1 (113)	1 (151)	2 (264)
Prevalence (95% CI)	0.8 [0-4.8]	0.6 [0-3.6]	0.7 [0-2.7]
Adjusted prevalence	0.29	0.22	0.25
10-14 years			
N. of cases (population size)	1 (142)	4 (231)	5 (373)
Prevalence (95% CI)	0.7 [0-3.8]	1.7 [0.4-4.3]	0.8 [0.1-2.3]
Adjusted prevalence	0.23	0.57	0.44
15-17 years			
N. of cases (population size)	0 (38)	0 (66)	0 (104)
Prevalence (95% CI)	0 [0-9.2]	0 [0-5.4]	0 [0-3.4]
Adjusted prevalence	0	0	0
Any age (5-17 years)			
N. of cases (population size)	2 (293)	5 (448)	7 (741)
Prevalence (95% CI)	0.68 [0.08-2.44]	1.11 [0.36-2.58]	0.94 [0.18-1.70]
Adjusted prevalence	0.52	0.79	0.69
Transient tic disorder			
6-9 years			
N. of cases (population size)	6 (113)	6 (151)	12 (264)
Prevalence (95% CI)	5.3 [0.73-9.80]	3.9 [0.52-7.42]	4.5 [1.84-7.24]

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Adjusted prevalence	1.76	1.32	1.51
10-14 years			
N. of cases (population size)	0 (142)	8 (231)	8 (373)
Prevalence (95% CI)	0 [0-2.5]	3.4 [0.8-6]	2.1 [0.5-3.7]
Adjusted prevalence	0	1.15	0.71
15-17 years			
N. of cases (population size)	0 (38)	0 (66)	0 (104)
Prevalence (95% CI)	0 [0-9.2]	0 [0-5.4]	0 [0-3.4]
Adjusted prevalence	0	0	0
Any age (5-17 years)			
N. of cases (population size)	6 (293)	14 (448)	20 (741)
Prevalence (95% CI)	2.04 [0.25-3.84]	3.12 [1.40-4.84]	2.69 [1.46-3.93]
Adjusted prevalence	1.76	2.47	2.23
Non-specified tic disorder			
6-9 years			
N. of cases (population size)	0 (113)	0 (151)	0 (264)
Prevalence (95% CI)	0 [0-3.21]	0 [0-2.41]	0 [0-1.38]
Adjusted prevalence	0	0	0
10-14 years			
N. of cases (population size)	2 (142)	1 (231)	3 (373)
Prevalence (95% CI)	1.4 [0.1-4.9]	0.4 [0.-2.3]	0.8 [0.1-2.3]
Adjusted prevalence	0.46	0.14	0.26
15-17 years			
N. of cases (population size)	1 (38)	0 (66)	1 (104)
Prevalence (95% CI)	2.6 [0-13.8]	0 [0-5.4]	0.9 [0-5.2]
Adjusted prevalence	0.87	0	0.32
Any age (5-17 years)			
N. of cases (population size)	3(293)	1 (448)	4 (741)
Prevalence (95% CI)	1.02 [0.21-2.96]	0.22 [0.00-1.23]	0.40 [0.08-1.17]
Adjusted prevalence	0.46	0.14	0.58