

Research article

Cross-sectional investigation of quality of life determinants among children with tic disorders: The roles of family environmental and clinical factors

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ABSTRACT

Objective: To examine the association between family environmental and clinical factors with the whole range of quality of life (QOL) in children with tic disorders (TD).

Methods: A hospital-based cross-sectional study was conducted among children with TD. All participants were given a family environmental survey and scale evaluations with Yale Global Tic Severity Scale (YGTSS), Achenbach Child Behavior Checklist (CBCL) and PedsQL-Generic Core Scale of the Chinese Version (PedsQL). Variable selection and data analysis was done by the least absolute shrinkage and selection operator (LASSO) method and multivariate logistic regression analysis.

Results: A total of 363 TD cases were included in the analysis. YGTSS scores, total CBCL score had significant negative correlations with PedsQL scores ($P < 0.05$). Of the total 15 factors, 8, 6, 11, 7, 5, 10 potential predictors with nonzero coefficients were identified by LASSO regression models of physical functioning, emotional functioning, social functioning, school functioning, social-psychological domain and PedsQL total scale respectively. Results of multivariate logistic regression analysis showed older age (physical functioning, ORs: 1.77, 3.67; total scale: ORs: 1.73, 2.28), no presence of chronic conditions (school functioning, OR: 1.61), moderate/severe tic severity (physical functioning, OR: 0.57; social functioning, OR: 0.44; social-psychological domain, OR: 0.57), co-morbid behavioral problems (physical functioning, OR: 0.52; emotional functioning, OR: 0.31; social functioning, OR: 0.30; school functioning, OR: 0.35; social-psychological domain, OR: 0.34; total scale, OR: 0.30), no fully parental involvement in care (physical functioning, OR: 0.62), higher paternal (physical functioning, ORs: 2.89, 2.07) and maternal education level (social functioning, ORs: 1.74, 2.03), democratic parenting pattern (emotional functioning, OR: 1.89; social functioning, OR: 2.17; social-psychological domain, OR: 2.33; total scale, OR: 2.11) and inharmony family relationship (emotional functioning, OR: 0.47; total scale, OR: 0.50) were the most important determinants to QOL of TD.

Conclusions: This study identifies several QOL determinants among children with TD. Clinicians should be encouraged to screen for family environmental and clinical factors in TD patients, and take tailored interventions to help TD children improve their QOL.

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1. Introduction

Tic disorders (TD) are multi-faceted neuropsychiatric disorders characterized by tics in the pediatric population with onset before the age of 18 years. Tics are sudden, repetitive, involuntary and stereotyped movements or vocalizations and vary in complexity, duration, intensity, and appearance [1]. Motor tics are rapid contraction of the fingers, face, neck, shoulders, trunk, and limbs. Vocal tics are the contraction of the oropharynx, throat, and respiratory muscles, and the sound is produced through the airflow in the nose, mouth and throat. The tics can be further divided into two categories: simple and complex, depending on the duration of tics and part (s) of body and group(s) of muscles involved. TD are divided into three types according to DSM-5: provisional tic disorder (PTD), chronic motor or vocal tic disorder (CTD), and Tourette syndrome (TS) [2]. The worldwide prevalence of TD in children was reported as ~6%, with PTD 2.99%, CTD 1.61%, and TS 0.77%, and more males than females [3,4]. TD are frequently comorbid with psychiatric symptoms and behavioral problems, such as attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), oppositional defiant disorder (ODD), autism spectrum disorders (ASD), depression, anxiety disorder and sleep disorders [5]. Tics and comorbidities have significant impairments in functioning in several life domains, such as social relations, academic, daily activities, school performance and might contribute to poor quality of life (QOL) of children and their families [6,7].

It is increasingly recognized that functional impairments in TD can be attributed to contextual factors, whether environmental or intrinsic [5]. However, studies exploring QOL in TD vary considerably in their clinical assessments; sample populations (TD vs. controls [6]; CTD vs. TS [7]; children vs. adults [6–8]); physical and mental aspects (tic severity [9], physical activity [10], psychiatric diagnoses [7,9,11], behavioral problems [12], etc.); QOL measure (generic [11,12] vs. disorder specific QOL [13]); interventions (peer attachment [14], modularized cognitive behavioral intervention [15], etc.); and statistical methodologies (multivariate analyses of variance [14], multiple regression analysis [6], mediation analyses [7], etc.). The impact of family environmental factors on TD patients' QOL is unclear and assessing simultaneously the independent effects of family environmental and clinical factors on QOL in children with TD has been rarely done. Additionally, it is not completely clear yet which aspects of QOL are more likely to be affected by these factors in TD. Furthermore, given the possible co-occurrence and co-variance, neglecting one or more of these factors in an analysis could inflate or deflate the statistical relevance of factors under consideration, leading to potentially inaccurate conclusions. Thus, to evaluate the association of factors with QOL from a multidimensional perspective and using appropriate multivariate analyses method are important for enhanced understanding of health-related QOL determinants in TD and targeted public health interventions.

The main aim of the current study was to examine the association of family environmental and clinical factors with the whole range of QOL in a hospital-based sample of children with TD. The Pediatric Quality of Life Inventory 4.0 (PedsQL) scale used in this study is a modular approach to measure health-related QOL in both healthy children and adolescents and in those with acute and chronic health conditions. Least absolute shrinkage and selection operator (LASSO) method was performed for variable selection and complexity regularization while fitting a generalized linear model [16,17]. Selective placement of variables into the multivariate analyses model can get better performance parameters and avoid overfitting. The results obtained in this study will have certain guiding significance for interventions, therapies, and the improvement of health and social care.

2. Methods

2.1. Participants and procedures

This is a hospital-based cross-sectional study. It was conducted in the outpatient Pediatrics Department of Renmin Hospital of Wuhan University from July 2019 to June 2022. This hospital is a large medical center and a regional teaching hospital in Hubei Province, with vast clinical services and a technological ability ranking among the top in China. Children aged 4–16 years who were the initial visited with a diagnosis of TD were consecutively recruited. The diagnosis of TD and types was according to the diagnostic schemes of DSM-5. All participants were given a family environmental survey and scale evaluations with Yale Global Tic Severity Scale (YGTSS), Achenbach Child Behavior Checklist (CBCL) and PedsQL-Generic Core Scale of the Chinese Version. Children were excluded for the following reasons: (1) had confirmed the following adverse mental or nervous conditions before the initial visit: schizophrenia, bipolar disorder, autism spectrum disorders, ADHD, OCD, intellectual disability and epilepsy; (2) refused to participate in this study; (3) incomplete or missing data on key variables, incorrect information or loss of contact.

For the estimation of sample size, three factors were set: a two-sided $\alpha = 0.05$, $\delta = 0.02$, and the prevalence of TD for children was set as 2% according to literature [18]. The sample size was calculated as 245 by PASS 15.0 software. Considering a potential drop-out rate of 20%, the targeted sample size is 307 children with TD.

The study was reported following the STROBE checklist. Before participating, participants provided written informed consent and/or permission for all research procedures. This study was performed according to the Declaration of Helsinki and research approval was obtained from the Clinical Research Ethics Committee of Renmin Hospital of Wuhan University (approval no. WDRY2022-K024).

2.2. Instruments and data collection

2.2.1. Clinical characteristics

The clinical characteristics were extracted from the Hospital Information System (HIS) by trained investigators. Presence of chronic conditions (not mental conditions) included but not restricted to allergic rhinitis, sinusitis, asthma, severe eczema, recurrent respiratory infections, conjunctivitis and enuresis. All children with tics were evaluated by physicians according to DSM-5 diagnostic

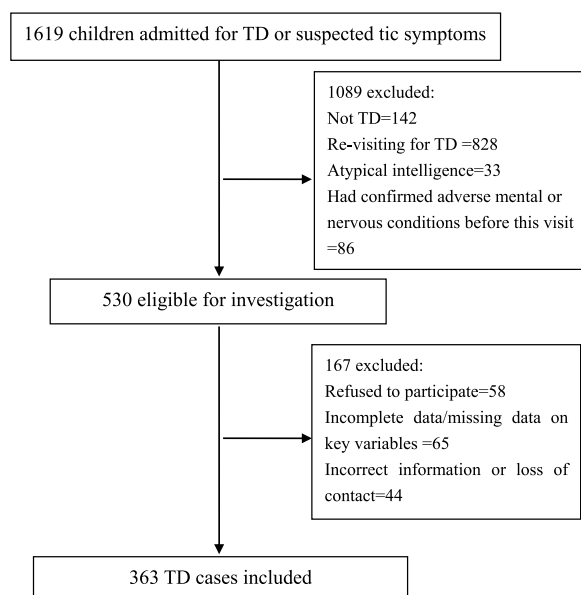


Fig. 1. Flow diagram of the study sample.

criteria: (i) PTD: has at least 1 motor tic and/or vocal tic, with a disease duration less than one year; (ii) CTD: only 1 form of motor or vocal tic appears during the course of the disease, with a duration longer than one year; (iii) TS: has multiple motor tics and 1 or more vocal tics, both of which might not appear at the same time, with a disease duration of more than one year. Symptom severity was measured by the YGTSS for tics.

2.2.2. Family environmental survey

During the initial ambulatory visit, an electronic questionnaire was completed by the child's main caregiver. A cover page gave information about the study, provided brief instructions, and an example of how to respond to the questions. This allowed us to generate family environmental variables: family structure (nuclear, stem and others), fully parental involvement in care (yes or no), paternal, maternal and other caregivers' education level (primary, secondary and university), parenting pattern (undemocratic or democratic), family relationship (harmony or inharmony) and family history (no TD/psychiatric disorders, parent/close relatives with TD, parent/close relatives with psychiatric disorders). The selection and evaluation of factors mainly refers to general appellations in sociology and previous literature [5]. Nuclear family refers to those which include parents and children only, while stem family refers to those which include parents, unmarried children, married sons and their wives. Parenting patterns are usually assessed in two dimensions: demand and responsiveness. Information on the two dimensions was obtained from the caregiver's report and two main parenting patterns were concluded: undemocratic, democratic. Family relationship was divided into harmony and inharmony, according to the self-evaluation of the caregivers.

2.2.3. YGTSS

The YGTSS is a clinician-rated semi-structured interview with demonstrated reliability and validity (Cronbach's α coefficient reaching 0.9) that measures tic symptom severity over the previous weeks [1]. The YGTSS produces a total tic score (range: 0–50, including motor tics and vocal tics), and a total impairment score (range: 0–50), with higher rating indicating greater tic severity. Motor tics and vocal tics scores are evaluated separately over the previous weeks from five dimensions: number, frequency, intensity, complexity, and interference with 0–5 score. The criteria for determining the tic severity are as follows: Total YGTSS score <25, mild; 25–50, moderate; and >50, severe [1].

2.2.4. CBCL

CBCL is a norm-referenced and widely used instrument in clinical practice and research to assess a variety of behavioral problems in children and adolescents. The parent-rated scale (CBCL-Chinese/4–18) was used in this study [19]. All parents completed CBCL during the initial ambulatory visit. Responses are coded as 0 (not true), 1 (somewhat or sometimes true), or 2 (very true or often true). In addition to a total score, eight empirically based syndrome scales and six DSM-oriented scales are reported. The score of any subscale or the total scale score equal to or above the 98th percentile was considered abnormal, indicating behavioral problems. The higher the score is, the more severe the child's behavioral problems are.

2.2.5. PedsQL-generic core scale of the Chinese Version

The PedsQL scale is a 23-item scale with higher scores corresponding to better children's QOL [12,20]. The following four subscales

Table 1
Family environmental and clinical variable characteristics of children with TD.

Variables	Statistics
<i>Clinical variables</i>	
Gender	
Male	291 (80.17)
Female	72 (19.83)
Age, years [median (IQR)]	7.57 (6.21,9.28)
Age distribution, years	
<6	76 (20.94)
6–10	222 (61.16)
>10	65 (17.91)
Presence of chronic conditions	
Yes	218 (60.06)
No	145 (39.94)
TD type	
PTD	284 (78.24)
CTD/TS	79 (21.76)
Tic form	
Simple motor/vocal tics	200 (55.10)
Complex tics	163 (44.90)
Tic severity	
Mild	248 (68.32)
Moderate/Severe	115 (31.68)
Co-morbid behavioral problems	
No	258 (71.07)
Yes	105 (28.93)
<i>Family environmental variables</i>	
Family structure	
Nuclear	151 (41.60)
Stem	193 (53.17)
Others (non-traditional)	19 (5.23)
Fully parental involvement in care	
Yes	178 (49.04)
No	185 (50.96)
Paternal education level	
Primary	78 (21.49)
Secondary	73 (20.11)
University	212 (58.40)
Maternal education level	
Primary	85 (23.42)
Secondary	63 (17.36)
University	215 (59.23)
Education level of other caregivers ^a	
Primary	93 (50.27)
Secondary	53 (28.65)
University	34 (18.38)
Unknown	5 (2.70)
Parenting pattern	
Undemocratic	241 (66.39)
Democratic	122 (33.61)
Family relationship	
Harmony	305 (84.02)
Inharmony	58 (15.98)
Family history	
No TD/psychiatric disorders	336 (92.56)
Parent/close relatives with TD	16 (4.41)
Parent/close relatives with psychiatric disorders	11 (3.03)

Results are presented as frequency (n) and percentage (%) for categorical variables.

^a Child had other one caregiver (n = 185).

have been identified: physical functioning (eight items), emotional functioning (five items), social functioning (five items) and school functioning (five items). Physical domain was composed of the eight items measured for physical functioning, while social-psychological domain was composed of the rest fifteen items measured for emotional functioning, social functioning and school functioning. Parent-proxy reports were used for our analyses. Parents rate the degree of problems or difficulties that the child experienced during the past month using a 5 Rating scale where 0 = never, 1 = almost never, 2 = sometime a problem, 3 = often a problem, 4 = almost always a problem. Items are reverse scored and linearly transformed to 0–100 (0 = 100, 1 = 75, 2 = 50, 3 = 25 and 4 = 0). The total scale score and subscale scores can be summed, divided by the number of included items. The total scale score and subscale scores of physical, emotional, social, school functioning and social-psychological domain was utilized as measures of QOL in our

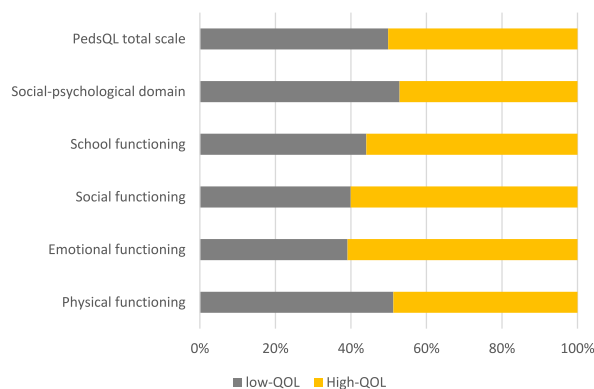


Fig. 2. 100% stacked bar chart of low-QOL and high-QOL percentages among children with TD according to the overall median values of the total scale score and subscale scores of PedsQL respectively (median split).

analyses. Reliability for the present sample was satisfactory (Cronbach's $\alpha = 0.894$ and split-half reliability $r = 0.723$).

2.3. Statistical analyses

Statistical analyses were performed with R software (version 4.2.1, <http://www.r-project.org/>). A listwise deletion approach (complete-case analysis) was used. Subjects with incomplete data/missing data for the variables included in the models were excluded. Continuous variables were presented as median and interquartile range (IQR). The total score and subscale scores of PedsQL were all as abnormal distribution by the Shapiro-Wilk test. Scores were dichotomization at the sample median and divided into low-QOL and high-QOL (called a median split) [21]. Categorical data were shown as frequencies and proportions and compared by Chi-square test (χ^2 test). The correlations between YGTSS scores, total CBCL score and PedsQL scores were tested with Spearman's correlation. The LASSO method was used to identify the most important predictive features with QOL of TD (binary discrete dependent variable, family = "binomial"). Features with nonzero coefficients in the LASSO regression model were selected into multivariate logistic regression analysis. Multivariate logistic regression analysis was performed to analyze the independent effects of factors on QOL of children (0 = low-QOL, 1 = high-QOL, with enter method). Results were reported as odds ratios (ORs) and 95% confidence interval (95%CI) for the explanatory variables. $P < 0.05$ was considered statistically significant (bilateral).

3. Results

The final analytic sample included 363 TD cases. A flow diagram of the 363 patients included in the study is provided in Fig. 1. Of the 363 participants, the majority was male (291/363, 80.17%), and the median age was 7.57 years old (IQR: 6.21, 9.28). The 8 family environmental and 7 clinical variables are listed in Table 1.

The median PedsQL total score and subscale scores of physical functioning, emotional functioning, social functioning and school functioning were 84.78 (IQR: 73.91, 92.39), 90.63 (IQR: 78.13, 100.00), 75.00 (IQR: 65.00, 95.00), 95.00 (IQR: 85.00, 100.00), 75.00 (IQR: 60.00, 90.00), respectively. The median score of social-psychological domain was 81.67 (IQR: 71.67, 90.00). The percentages of low-QOL and high-QOL are shown in Fig. 2. The PedsQL scores in different groups of family environmental and clinical variables are presented in Table 2.

The correlations between YGTSS scores, total CBCL score and PedsQL scores are shown in Fig. 3. Results showed that YGTSS scores and total CBCL score had undoubted significant negative correlations with PedsQL scores ($P < 0.05$). Tree diagram also indicated good validity of the YGTSS and PedsQL scale for the present sample (Fig. 3).

Of the total 15 key variables, 8, 6, 11, 7, 5, 10 potential predictors with nonzero coefficients were identified by the LASSO regression models of physical functioning, emotional functioning, social functioning, school functioning, social-psychological domain and PedsQL total scale respectively (Fig. 4A–F, Fig. 5A–F, Table 3). These predictors were then selected into multivariate logistic regression analysis.

The results of multivariate logistic regression analysis present the adjusted association estimates between these predictors and high-QOL in children with TD. Slight variations in the point estimate and statistical significance were noted when family environmental factors were entered (from Model 1 to Model 2, seen in Table 4). Results showed that (1) QOL in physical functioning: older age (ORs: 1.77, 3.67) and higher paternal education level (ORs: 2.89, 2.07) predicted higher QOL. Moderate/severe tic severity (OR: 0.57), co-morbid behavioral problems (OR: 0.52) and no fully parental involvement in care (OR: 0.62) predicted lower QOL. (2) QOL in emotional functioning: democratic parenting pattern (OR: 1.89) predicted higher QOL. Co-morbid behavioral problems (OR: 0.31) and inharmony family relationship (OR: 0.47) predicted lower QOL. (3) QOL in social functioning: higher maternal education level (ORs: 1.74, 2.03) and democratic parenting pattern (OR: 2.17) predicted higher QOL. Moderate/severe tic severity (OR: 0.44) and co-morbid behavioral problems (OR: 0.30) predicted lower QOL. (4) QOL in school functioning: no presence of chronic conditions predicted higher QOL (OR: 1.61). Co-morbid behavioral problems (OR: 0.35) predicted lower QOL. (5) QOL in social-psychological domain:

Table 2
PedsQL scores [median (IQR)] in different groups of family environmental and clinical variables.

	Physical functioning	Emotional functioning	Social functioning	School functioning	Social-psychological domain	PedsQL total scale score
<i>Overall</i>	90.63 (78.13, 100.00)	75.00 (65.00, 95.00)	95.00 (85.00, 100.00)	75.00 (60.00, 90.00)	81.67 (71.67, 90.00)	84.78 (73.91, 92.39)
Gender						
Male	90.63 (78.13,100.00)	75.00 (60.00,95.00)	95.00 (80.00,100.00)	75.00 (60.00,86.67)	81.67 (70.00,90.00)	83.70 (73.91,91.30)
Female	93.75 (77.34,100.00)	80.00 (68.75,96.25)	97.50 (85.00,100.00)	80.00 (65.00,90.00)	85.00 (73.33,93.33)	86.96 (75.00,92.39)
Age, years						
<6	87.50 (78.13,93.75)	75.00 (65.00,90.00)	95.00 (85.00,100.00)	75.00 (65.00,85.00)	81.67 (71.67,90.00)	83.15 (73.91,91.30)
6–10	90.63 (75.00,100.00)	80.00 (65.00,95.00)	95.00 (85.00,100.00)	77.50 (60.00,90.00)	81.67 (70.00,90.00)	84.78 (74.18,92.39)
>10	93.75 (83.38,100.00)	85.00 (60.00,100.00)	100.00 (75.00,100.00)	70.00 (55.00,85.00)	80.00 (68.33,91.67)	85.87 (76.09,92.39)
Presence of chronic conditions						
Yes	90.63 (78.13,100.00)	75.00 (60.00,90.00)	95.00 (80.00,100.00)	75.00 (60.00,85.00)	80.00 (70.00,90.00)	83.70 (72.83,91.30)
No	93.75 (75.00,100.00)	80.00 (70.00,95.00)	95.00 (85.00,100.00)	80.00 (65.00,90.00)	83.33 (75.00,91.67)	85.87 (76.09,92.39)
TD type						
PTD	93.75 (78.13,100.00)	80.00 (65.00,95.00)	95.00 (85.00,100.00)	75.00 (60.00,90.00)	81.67 (71.67,90.00)	84.78 (75.00,92.39)
CTD/TS	87.50 (78.13,100.00)	75.00 (60.00,90.00)	95.00 (82.50,100.00)	75.00 (60.00,89.17)	81.67 (65.00,89.17)	83.70 (71.20,89.13)
Tic form						
Simple motor/vocal tics	93.75 (78.13,100.00)	85.00 (70.00,100.00)	100.00 (88.75,100.00)	75.00 (65.00,90.00)	83.33 (75.00,92.08)	85.87 (77.17,93.48)
Complex tics	87.50 (76.56,96.88)	75.00 (60.00,87.50)	95.00 (75.00,100.00)	75.00 (55.00,86.67)	78.33 (66.67,88.33)	81.52 (70.65,89.13)
Tic severity						
Mild	93.75 (81.25,100.00)	80.00 (70.00,100.00)	100.00 (90.00,100.00)	77.50 (65.00,90.00)	83.33 (75.00,91.67)	85.87 (78.26,93.48)
Moderate/Severe	87.50 (73.44,93.75)	70.00 (55.00,85.00)	90.00 (75.00,100.00)	70.00 (55.00,85.00)	76.67 (65.00,85.83)	78.26 (69.02,86.96)
Co-morbid behavioral problems						
No	93.75 (81.25,100.00)	85.00 (70.00,100.00)	100.00 (90.00,100.00)	80.00 (65.00,90.00)	85.00 (76.67,93.33)	86.96 (79.35,93.48)
Yes	81.25 (68.75,96.88)	65.00 (55.00,80.00)	85.00 (70.00,100.00)	65.00 (50.00,80.00)	70.00 (60.00,81.67)	75.00 (63.04,85.87)
Family structure						
Nuclear	93.75 (78.13,100.00)	80.00 (65.00,95.00)	95.00 (85.00,100.00)	75.00 (60.00,90.00)	83.33 (72.50,90.83)	85.87 (75.54,92.39)
Stem	87.50 (78.13,100.00)	75.00 (65.00,90.00)	95.00 (80.00,100.00)	75.00 (60.00,90.00)	81.67 (70.00,90.00)	83.70 (73.91,91.30)
Others (non-traditional)	93.75 (78.13,96.88)	70.00 (60.00,100.00)	100.00 (90.00,100.00)	70.00 (55.00,80.00)	81.67 (68.33,88.33)	86.96 (71.20,90.76)
Fully parental involvement in care						
Yes	93.75 (81.25,100.00)	80.00 (65.00,95.00)	100.00 (85.00,100.00)	75.00 (60.00,90.00)	84.17 (73.33,90.17)	85.87 (77.17,92.39)
No	87.50 (75.00,100.00)	75.00 (60.00,95.00)	95.00 (80.00,100.00)	75.00 (60.00,85.00)	80.00 (70.00,90.00)	81.52 (72.83,91.30)
Paternal education level						
Primary	82.81 (69.53,93.75)	75.00 (60.00,90.00)	90.00 (75.00,100.00)	70.00 (51.25,80.00)	78.33 (65.00,87.92)	79.89 (69.57,86.96)
Secondary	93.75 (78.13,100.00)	75.00 (65.00,100.00)	100.00 (85.00,100.00)	75.00 (65.00,90.00)	81.67 (71.67,93.33)	85.87 (73.91,93.48)
University	93.75 (80.47,100.00)	80.00 (65.00,91.25)	100.00 (85.00,100.00)	80.00 (65.00,90.00)	82.50 (73.33,91.67)	85.87 (76.09,92.39)
Maternal education level						
Primary	87.50 (75.00,100.00)	80.00 (65.00,95.00)	90.00 (75.00,100.00)	75.00 (60.00,85.00)	81.67 (66.67,88.33)	81.52 (71.74,91.30)
Secondary	93.75 (73.44,100.00)	75.00 (60.00,95.00)	95.00 (80.00,100.00)	70.00 (55.00,85.00)	78.33 (68.33,89.17)	85.87 (69.57,89.67)
University	90.63 (78.13,100.00)	80.00 (65.00,95.00)	100.00 (85.00,100.00)	80.00 (65.00,90.00)	81.67 (73.33,91.67)	85.87 (76.09,92.39)
Education level of other caregivers						

(continued on next page)

Table 2 (continued)

	Physical functioning	Emotional functioning	Social functioning	School functioning	Social-psychological domain	PedsQL total scale score
Primary	87.50 (75.00,95.31)	75.00 (60.00,90.00)	95.00 (85.00,100.00)	75.00 (55.00,85.00)	78.33 (66.67,89.17)	81.52 (71.20,88.59)
Secondary	87.50 (75.00,100.00)	80.00 (65.00,95.00)	95.00 (77.50,100.00)	75.00 (65.00,87.50)	81.67 (70.00,91.67)	82.61 (72.83,92.93)
University	87.50 (74.22,100.00)	80.00 (68.75,92.50)	95.00 (80.00,100.00)	70.00 (60.00,85.00)	81.67 (71.25,88.33)	79.35 (72.83,91.30)
Parenting pattern						
Undemocratic	87.50 (75.00,100.00)	75.00 (60.00,90.00)	95.00 (75.00,100.00)	75.00 (55.00,85.00)	78.33 (66.67,88.33)	81.52 (71.74,89.13)
Democratic	93.75 (81.25,100.00)	85.00 (75.00,100.00)	100.00 (95.00,100.00)	80.00 (65.00,90.00)	86.67 (77.08,93.33)	89.13 (79.62,93.48)
Family relationship						
Harmony	93.75 (78.13,100.00)	80.00 (65.00,95.00)	100.00 (85.00,100.00)	75.00 (60.00,90.00)	83.33 (71.67,91.67)	85.87 (75.00,92.39)
Inharmony	87.50 (72.66,99.22)	67.50 (60.00,88.75)	87.50 (70.00,100.00)	75.00 (55.00,85.00)	76.67 (65.00,83.33)	78.80 (69.57,85.87)
Family history						
No TD/psychiatric disorders	90.63 (78.13,100.00)	80.00 (65.00,95.00)	95.00 (85.00,100.00)	75.00 (60.00,90.00)	81.67 (71.67,90.00)	84.78 (73.91,92.39)
Parent/close relatives with TD	90.63 (85.94,97.66)	77.50 (65.00,85.00)	97.50 (83.75,100.00)	75.00 (58.75,85.00)	80.83 (75.83,85.42)	83.15 (78.53,87.50)
Parent/close relatives with psychiatric disorders	81.25 (68.75,93.75)	65.00 (60.00,72.50)	90.00 (75.00,100.00)	75.00 (62.50,77.50)	75.00 (67.50,80.83)	77.17 (66.30,85.33)

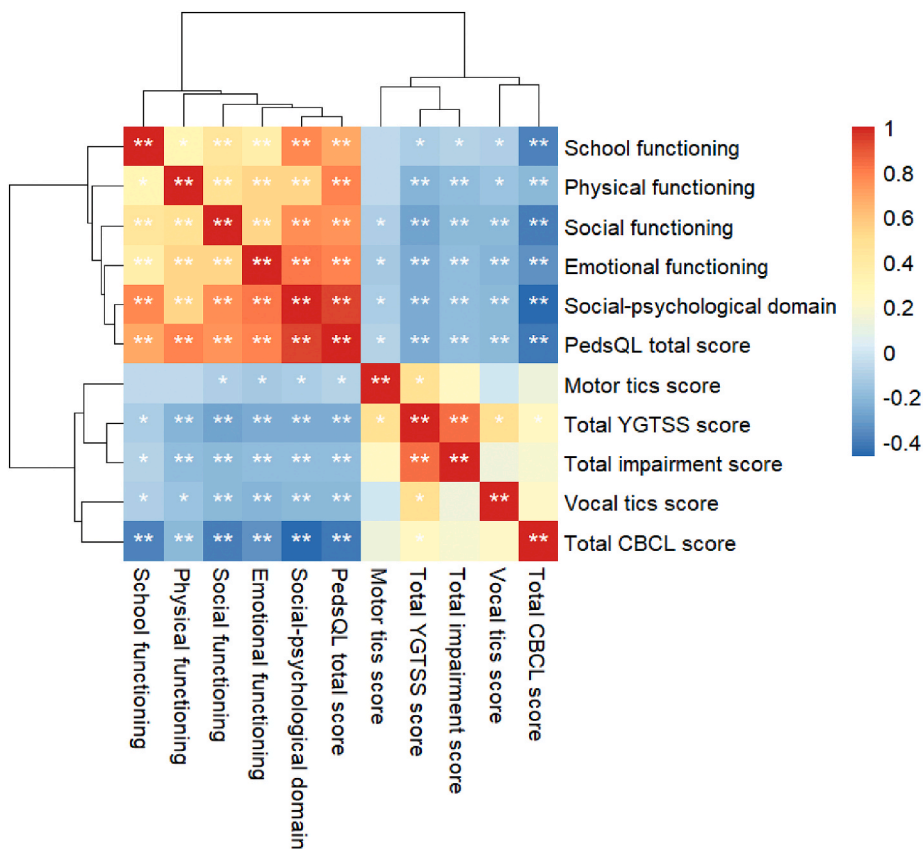


Fig. 3. Heatmap based on the Spearman's correlation matrix of YGTSS scores, total CBCL score and PedsQL scores (*P < 0.05, **P < 0.01). Colors indicate positive correlations (red, yellow) or negative correlations (blue) of the given variables.

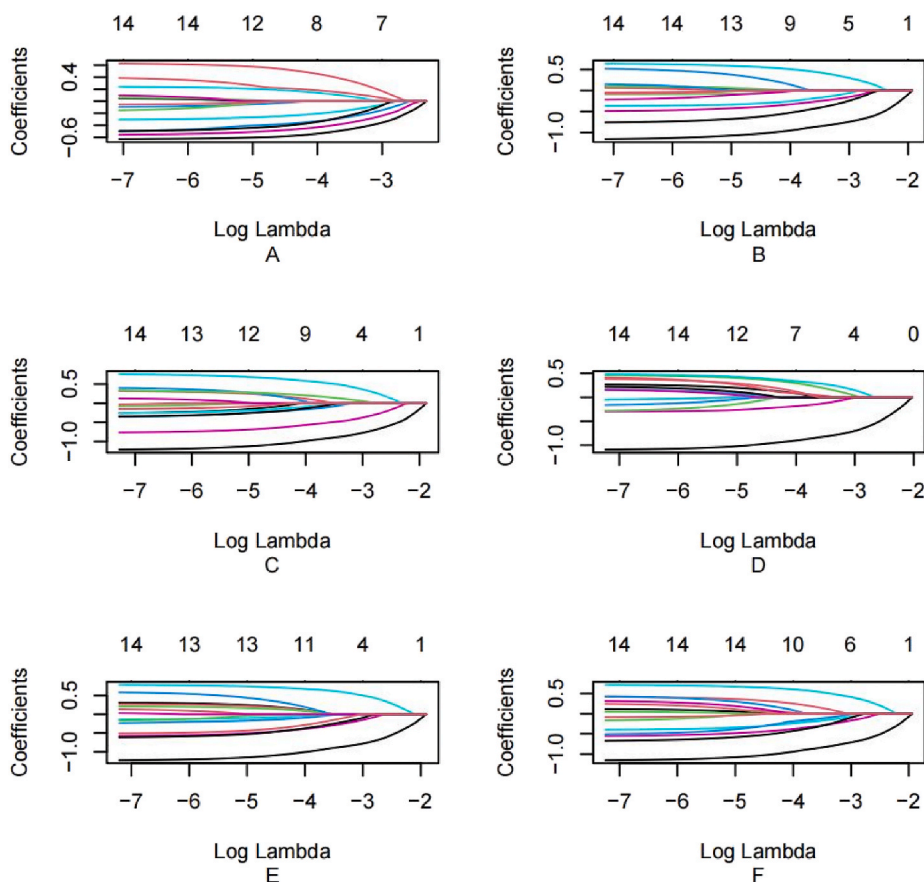


Fig. 4. LASSO coefficient profiles of the 15 variables in (A) physical functioning, (B) emotional functioning, (C) social functioning, (D) school functioning, (E) social-psychological domain and (F) PedsQL total scale score. A coefficient profile plot was produced against the $\log(\lambda)$ sequence. Each curve represents the change of each independent variable coefficient. The ordinate is the value of the coefficient, the lower abscissa is $\log(\lambda)$, and the upper abscissa is the number of nonzero coefficients in the model at this time.

democratic parenting pattern (OR: 2.33) predicted higher QOL. Moderate/severe tic severity (OR: 0.57) and co-morbid behavioral problems (OR: 0.34) predicted lower QOL. (6) QOL in total scale: older age (ORs: 1.73, 2.28) and democratic parenting pattern (OR: 2.11) predicted higher QOL. Co-morbid behavioral problems (OR: 0.30) and inharmony family relationship (OR: 0.50) predicted lower QOL.

4. Discussion

QOL is recognized as an important health outcome measurement for pediatric patients. The purpose of this study was to elucidate the association of family environmental and clinical factors with QOL among children with TD. Results of multivariate logistic regression analysis showed age, presence of chronic conditions, tic severity, co-morbid behavioral problems, fully parental involvement in care, paternal and maternal education level, parenting pattern and family relationship were the most important determinants to QOL of TD. For clinicians and patients' families, understanding the factors that determine QOL of TD can provide insight into developing more targeted interventions.

PedsQL scale is widely used for the evaluation of children's health-related QOL. It integrates generic core scale and disease-specific modules. Since the disease-specific modules have not included TD, we used the generic core scale of the Chinese version, which is used for measuring the common part of QOL in children aged 2–18 years with good reliability and validity [20]. In this study the scale also has satisfactory reliability and validity in the QOL evaluation of children with TD. In the current study, the scores of emotional functioning and school functioning were the lowest, and the score of social-psychological domain was lower than the score of physical domain, which is consistent with previous researches [14,22].

Various family environmental and clinical factors were explored in this study. The factors investigated in the present study mainly refer to previous studies of childhood neuropsychiatric/psychiatric disorders and general population [23,24,25,26]. Results of the different groups of family environmental and clinical variables indicated female, older age, no presence of chronic conditions, nuclear family structure, higher paternal and maternal education level, democratic parenting pattern had relatively higher PedsQL scores.

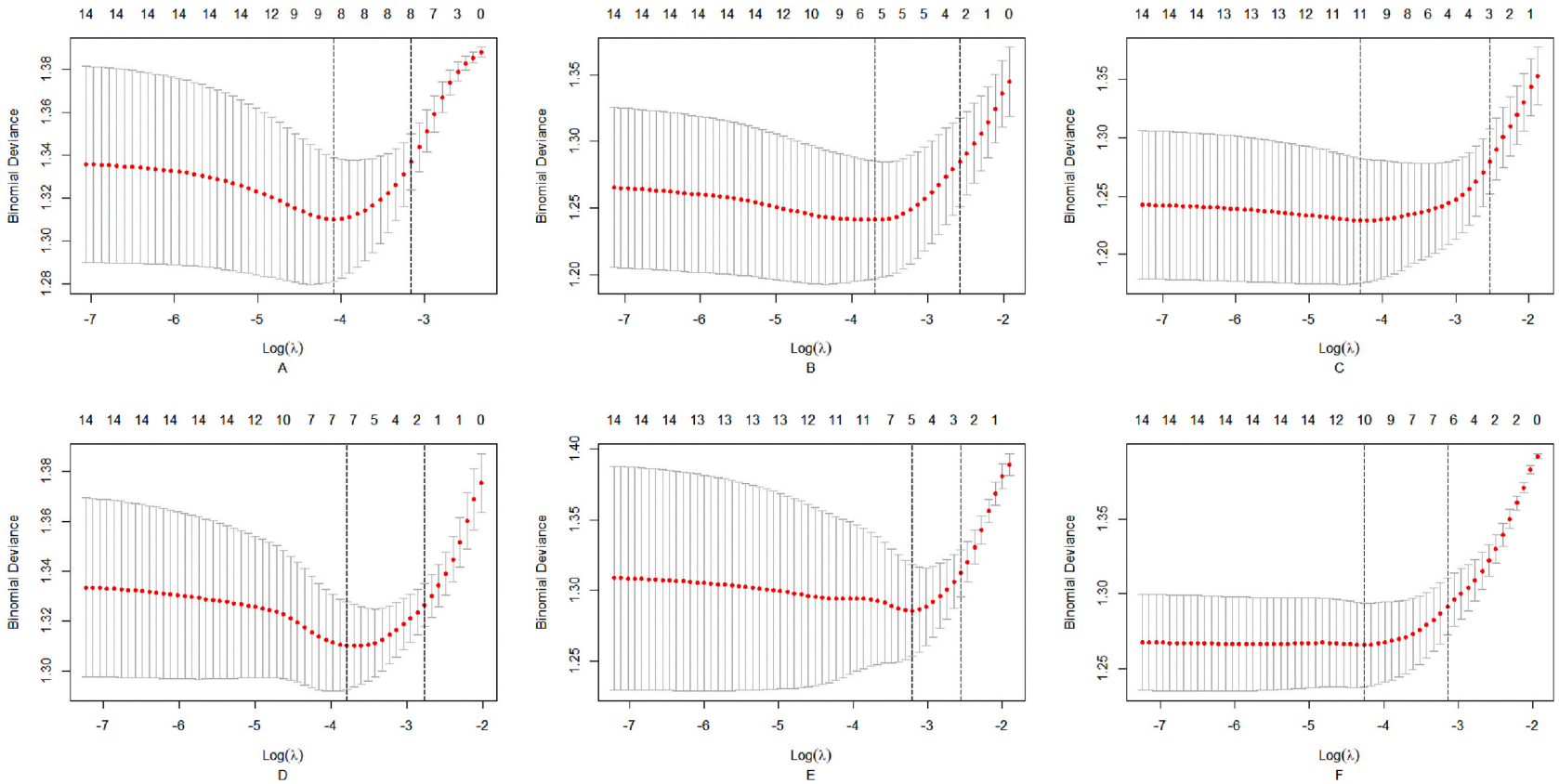


Fig. 5. Optimal parameter (λ) selection in the LASSO models of (A) physical functioning, (B) emotional functioning, (C) social functioning, (D) school functioning, (E) social-psychological domain and (F) PedsQL total scale score used fivefold cross-validation via minimum criteria. The binomial deviance curve was plotted versus $\log(\lambda)$. The ordinate is binomial deviance, the lower abscissa is $\log(\lambda)$, and the upper abscissa is the number of features (variables) in the model at this time. Two dotted vertical lines were drawn at the optimal values by using the minimum criteria and the 1 SE of the minimum criteria (the 1-SE criteria). We selected predictive features using the minimum criteria (the left vertical line).

Table 3
Potential predictors identified by the LASSO regression models.

	Predictor number	Potential predictors
Physical functioning	8	Age, tic form, tic severity, co-morbid behavioral problems, fully parental involvement in care, paternal education level, parenting pattern, family relationship
Emotional functioning	6	TD type, tic form, tic severity, co-morbid behavioral problems, parenting pattern, family relationship
Social functioning	11	Gender, age, TD type, tic form, tic severity, co-morbid behavioral problems, fully parental involvement in care, maternal education level, parenting pattern, family relationship, family history
School functioning	7	Gender, presence of chronic conditions, tic severity, co-morbid behavioral problems, paternal education level, parenting pattern, family history
Social-psychological domain	5	Tic severity, co-morbid behavioral problems, parenting pattern, family relationship, family history
PedsQL total scale	10	Age, TD type, tic form, tic severity, co-morbid behavioral problems, family structure, fully parental involvement in care, paternal education level, parenting pattern, family relationship

CTD/TS, complex tics, moderate/severe tic severity, co-morbid behavioral problems, no fully parental involvement in care, inharmony family relationship and parent/close relatives with psychiatric disorders had relatively lower PedsQL scores. In order to analyze the independent effects of family environmental and clinical variables on QOL in children with TD, and also because of most of these variables were categorical variables, we dichotomized the continuous dependent variables-PedsQL scores via the median split procedure [21]. Then we used the LASSO regression model to build a risk factor classifier before multivariate logistic regression analysis. LASSO regression is a data dimension reduction method, which enables researchers to identify pertinent and exclude irrelevant predictors, regardless of the target dependent variable is continuous, or binary/multivariate discrete [17]. It selects variables from the sample based on a penalty method. If the original coefficients are directly compressed to 0, the variables corresponding to these coefficients are regarded as non-significant variables and discarded directly. After the LASSO regression analysis in the present study, 8, 6, 11, 7, 5, 10 potential predictors with nonzero coefficients in the models of physical functioning, emotional functioning, social functioning, school functioning, social-psychological domain and PedsQL total scale respectively were selected.

Results of multivariate logistic regression analysis showed that family environmental factors such as fully parental involvement in care, paternal and maternal education level, parenting pattern and family relationship were the most important predictive features with QOL of TD. Fully parental involvement in care and higher paternal education level predicted higher QOL in physical functioning, higher maternal education level predicted higher QOL in social functioning, and harmony family relationship predicted higher QOL in physical functioning and the total scale, while democratic parenting pattern predicted higher QOL in emotional functioning, social functioning, social-psychological domain and the total scale. The findings are in line with previous studies among general population [27,28]. There are several possible explanations for these independent associations. First, parenting pattern and parental involvement in care changes might influence conversation time and parent-child interactions [23]. Second, inadequate parenting, such as over involvement, and excessive control, fosters a hostile and self-esteem neglectful environment for the child and inhibit their abilities to appropriately self-regulate behaviors and emotions [29]. Third, parental education level reflects the social-economic status of the family to a certain extent. Parents with high educational level can give children better guidance in study and life [24]. Therefore, an integrated health education programme for caregivers should strengthen parental involvement in care and democratic parenting pattern, and targeted interventions should specifically meet the needs of non-parent caregivers so as to improve the QOL of children with TD. Nevertheless, the role of family environmental factors on the QOL of children with TD remains to be confirmed by more longitudinal studies with large samples in the future.

As demonstrated in previous researches [7,14], presence of chronic conditions, increased tic severity and co-morbid behavioral problems predicted adverse outcomes and was associated with lower QOL. The present findings also identified the significant relationship between YGTSS scores, total CBCL score and PedsQL scores. Results of multivariate logistic regression analysis showed that no presence of chronic conditions predicted higher QOL in school functioning, and moderate/severe tic severity predicted lower QOL in physical functioning, social functioning and social-psychological domain. Whilst co-morbid behavioral problems were the strongest predictive effects reported for all measured parts of PedsQL. As already known, TD are highly comorbid with behavioral problems, such as ADHD, OCD, ODD, etc. Consistent with our findings, Huisman-van Dijk et al. found comorbidities can directly and indirectly affect the QOL of children with TD by mediation analyses [24]. This highlights the importance of investigating comorbidities in TD in concert to unravel their combined effects on QOL. In line with and extending previous studies, our findings showed that co-morbid behavioral problems affect all aspects of QOL and its predictive effects beyond tic severity in every detailed aspect. Regarding the high percentage of comorbidities in clinical patients with TD, much more attention should be given to reduce the impairment of comorbidities, strengthen behavioral interventions, and provide supports for children's family, school, community and peer relationships in order to improve the QOL of children with TD, instead of focusing on reducing the tics themselves.

To our knowledge, the investigation of QOL determinants among children with TD in China is rare. Our results indicated the QOL of children with TD affected by many factors, including not only clinical factors but also the family environmental factors. Therefore, to enhance the QOL of children with TD, in addition to reduce tics themselves, it should take psychological and behavioral interventions, and pay attention to improve the poor family environment, such as no fully parental involvement in care, undemocratic parenting pattern, and inharmony family relationship, thus further reduce the negative impact of these factors on children's QOL.

Table 4
Multivariate logistic regression analysis: association of selected family environmental and clinical factors with QOL of TD.

	Model 1			Model 2		
	OR	95%CI	P	OR	95%CI	P
<i>Physical functioning</i>						
Age, years						
<6	Ref			Ref		
6–10	1.79	1.03–5.95	0.040	1.77	1.01–3.16	0.049
>10	3.48	1.70–7.32	0.001	3.67	1.71–8.08	0.001
Tic form						
Simple motor/vocal tics	Ref			Ref		
Complex tics	0.72	0.46–1.15	0.167	0.70	0.44–1.13	0.147
Tic severity						
Mild	Ref			Ref		
Moderate/Severe	0.53	0.32–0.89	0.016	0.57	0.33–0.96	0.035
Co-morbid behavioral problems						
No	Ref			Ref		
Yes	0.43	0.26–0.71	0.001	0.52	0.30–0.87	0.014
Fully parental involvement in care						
Yes				Ref		
No				0.62	0.39–0.98	0.039
Paternal education level						
Primary				Ref		
Secondary				2.89	1.42–6.00	0.004
University				2.07	1.15–3.82	0.017
Parenting pattern						
Undemocratic				Ref		
Democratic				1.33	0.82–2.19	0.252
Family relationship						
Harmony				Ref		
Inharmony				0.63	0.32–1.20	0.165
<i>Emotional functioning</i>						
TD type						
PTD	Ref			Ref		
CTD/TS	1.59	0.89–2.89	0.122	1.66	0.92–3.09	0.099
Tic form						
Simple motor/vocal tics	Ref			Ref		
Complex tics	0.65	0.40–1.05	0.079	0.66	0.40–1.07	0.091
Tic severity						
Mild	Ref			Ref		
Moderate/Severe	0.60	0.36–1.01	0.053	0.63	0.37–1.06	0.078
Co-morbid behavioral problems						
No	Ref			Ref		
Yes	0.28	0.16–0.46	<0.001	0.31	0.18–0.53	<0.001
Parenting pattern						
Undemocratic				Ref		
Democratic				1.89	1.13–3.22	0.016
Family relationship						
Harmony				Ref		
Inharmony				0.47	0.25–0.89	0.021
<i>Social functioning</i>						
Gender						
Male	Ref			Ref		
Female	0.85	0.48–1.51	0.569	0.76	0.42–1.38	0.360
Age, years						
<6	Ref			Ref		
6–10	1.13	0.63–1.99	0.687	1.16	0.64–2.10	0.616
>10	1.60	0.76–3.42	0.218	1.99	0.90–4.51	0.094
TD type						
PTD	Ref			Ref		
CTD/TS	1.46	0.82–2.66	0.206	1.60	0.87–3.00	0.136
Tic form						
Simple motor/vocal tics	Ref			Ref		
Complex tics	0.78	0.48–1.28	0.326	0.77	0.47–1.28	0.309
Tic severity						
Mild	Ref			Ref		
Moderate/Severe	0.43	0.25–0.72	0.001	0.44	0.25–0.75	0.003
Co-morbid behavioral problems						
No	Ref			Ref		
Yes	0.26	0.15–0.44	<0.001	0.30	0.17–0.52	<0.001
Fully parental involvement in care						

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Table 4 (continued)

	Model 1			Model 2		
	OR	95%CI	P	OR	95%CI	P
Yes				Ref		
No				0.75	0.46–1.21	0.241
Maternal education level						
Primary				Ref		
Secondary				1.74	0.84–3.68	0.139
University				2.03	1.14–3.62	0.016
Parenting pattern						
Undemocratic				Ref		
Democratic				2.17	1.27–3.77	0.005
Family relationship						
Harmony				Ref		
Inharmony				0.70	0.36–1.35	0.283
Family history						
No TD/psychiatric disorders				Ref		
Parent/close relatives with TD				1.46	0.44–4.97	0.537
Parent/close relatives with psychiatric disorders				0.51	0.11–2.02	0.350
School functioning						
Gender						
Male	Ref			Ref		
Female	1.37	0.79–2.41	0.274	1.32	0.75–2.35	0.342
Presence of chronic conditions						
Yes	Ref			Ref		
No	1.58	1.02–2.49	0.043	1.61	1.02–2.55	0.043
Tic severity						
Mild	Ref			Ref		
Moderate/Severe	0.71	0.44–1.15	0.160	0.75	0.46–1.23	0.256
Co-morbid behavioral problems						
No	Ref			Ref		
Yes	0.34	0.21–0.55	<0.001	0.35	0.21–0.57	<0.001
Paternal education level						
Primary				Ref		
Secondary				1.64	0.83–3.26	0.155
University				1.51	0.86–2.66	0.151
Parenting pattern						
Undemocratic				Ref		
Democratic				1.58	0.98–2.58	0.064
Family history						
No TD/psychiatric disorders				Ref		
Parent/close relatives with TD				1.24	0.41–3.79	0.702
Parent/close relatives with psychiatric disorders				2.43	0.66–10.02	0.189
Social-psychological domain						
Tic severity						
Mild	Ref			Ref		
Moderate/Severe	0.55	0.34–0.90	0.017	0.57	0.34–0.94	0.027
Co-morbid behavioral problems						
No	Ref			Ref		
Yes	0.27	0.16–0.46	<0.001	0.34	0.19–0.57	<0.001
Parenting pattern						
Undemocratic				Ref		
Democratic				2.33	1.43–3.81	0.001
Family relationship						
Harmony				Ref		
Inharmony				0.59	0.29–1.15	0.124
Family history						
No TD/psychiatric disorders				Ref		
Parent/close relatives with TD				1.06	0.32–3.35	0.916
Parent/close relatives with psychiatric disorders				0.18	0.01–1.03	0.111
PedsQL total scale						
Age, years						
<6	Ref			Ref		
6–10	1.70	0.98–3.00	0.061	1.73	0.97–3.10	0.063
>10	2.14	1.04–4.47	0.041	2.28	1.05–5.03	0.038
TD type						
PTD	Ref			Ref		
CTD/TS	1.51	0.86–2.72	0.159	1.60	0.88–2.97	0.129
Tic form						
Simple motor/vocal tics	Ref			Ref		
Complex tics	0.68	0.42–1.08	0.102	0.64	0.39–1.05	0.076

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Table 4 (continued)

	Model 1			Model 2		
	OR	95%CI	P	OR	95%CI	P
Tic severity						
Mild	Ref			Ref		
Moderate/Severe	0.55	0.32–0.92	0.024	0.58	0.34–1.00	0.051
Co-morbid behavioral problems						
No	Ref			Ref		
Yes	0.26	0.15–0.44	<0.001	0.30	0.17–0.52	<0.001
Family structure						
Nuclear				Ref		
Stem				1.22	0.68–2.22	0.497
Others (non-traditional)				2.47	0.78–8.02	0.125
Fully parental involvement in care						
Yes				Ref		
No				0.62	0.35–1.09	0.097
Paternal education level						
Primary				Ref		
Secondary				1.76	0.86–3.65	0.126
University				1.42	0.78–2.60	0.252
Parenting pattern						
Undemocratic				Ref		
Democratic				2.11	1.28–3.52	0.004
Family relationship						
Harmony				Ref		
Inharmony				0.50	0.25–0.99	0.049

Model 1 included clinical factors only; Model 2 included clinical and family environmental factors.

OR odds ratio, CI confidence interval, Ref as reference.

5. Study limitations

Some important limitations should be considered. First, the cross-sectional design of this study limited our ability to draw conclusions about the causal relationship between QOL and the associated factors. Second, analysis of a single center sample of patients may limit generalizations to other clinical units or populations. Additionally, family environmental information was mainly reliance on reports of child's main caregiver. This may contribute to reporting bias. Third, QOL of TD patients may be affected by multiple factors. We did not have a control group to explore the effects of tics themselves on QOL. Besides this, although we examined a broad range of factors, some factors that may affect QOL of TD remain unmeasured.

6. Conclusion

Collectively, our findings highlight the role of family environmental and clinical factors in connecting the whole range of QOL in children with TD. Age, presence of chronic conditions, tic severity, co-morbid behavioral problems, fully parental involvement in care, paternal and maternal education level, parenting pattern and family relationship were the most important determinants to QOL of TD. The results should encourage clinicians to screen for these factors in children with TD, and there is a need for tailored interventions to help TD children improve their QOL accordingly.

Author contribution statement

Fang Liu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Gaohua Wang: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Baozhen Yao: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data.

Jingping Ye: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Junling Wang: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Huaqian Wang: Performed the experiments; Wrote the paper.

Hong Liu: Performed the experiments; Contributed reagents, materials, analysis tools or data.

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Data availability statement

Data included in article/supp. Material/referenced in article.

Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2023.e13228>.

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