


# BMJ Open Prevalence of nail biting and its chronological relationship with tics in child and adolescent outpatients with Tourette syndrome: a single-centre, retrospective observational study

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## ABSTRACT

**Objective** To evaluate the prevalence of nail biting in child and adolescent outpatients at a single institution and the chronological relationship between nail biting and tics in patients with Tourette syndrome (TS) with or without attention-deficit hyperactivity disorder (ADHD).

**Design** Retrospective observational study.

**Setting** Teaching hospital in Taiwan.

**Participants** All participants were aged 4–18 years, including 535 patients with TS, 230 patients with provisional tic disorder and 1460 patients without neurological or psychiatric disorders (controls).

**Outcome measures** Presence of nail biting, starting age for nail biting and starting age for motor and/or vocal tics.

**Results** Nail biting was more commonly observed in patients with TS (56.6%) than in patients with provisional tic disorder (27.4%) or controls (15.0%), regardless of sex (all  $p < 0.020$ ). Nail biting was also more common in patients with TS with ADHD than in those without (75.0% vs 47.6%;  $p < 0.001$ ), but the starting age was significantly later in those with concomitant ADHD than without (5.3 vs 3.8 years;  $p < 0.001$ ). In patients with TS, the onset of nail biting occurred earlier than that of tics, regardless of ADHD status.

**Conclusion** Nail biting was more prevalent and occurred earlier than tics in patients with TS, regardless of ADHD status, in the study population.

## INTRODUCTION

Tourette syndrome (TS) is a chronic neurodevelopmental disorder hallmarked by vocal or motor tics with a propensity to affect children.<sup>1</sup> TS affects an estimated 6 per 1000 children worldwide and 5.6 per 1000 children aged 6–12 years in Taiwan.<sup>2,3</sup> The ratio of men to women in Taiwanese TS children is approximately 4.5:1.<sup>2</sup> The presence of tic disorder is a typical but non-specific symptom of TS, as it can occur in other autism-spectrum disease entities.<sup>1</sup> Tics also may occur transiently and resolve within 1 year, hence the term ‘provisional tic disorder’ for such conditions.<sup>1,4</sup> The diagnosis of TS is primarily observational

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The study was conducted in a large cohort.
- ⇒ The time interval between the onset of nail biting and tics in patients with Tourette syndrome (TS) was stratified according to both age and sex.
- ⇒ Data analysis distinguishes between patients with TS alone and those with TS and attention-deficit hyperactivity disorder.
- ⇒ The generalisability of the results is limited by the single-centre setting, retrospective design, small number of girls aged  $\geq 13$  years and inclusion of only hospital outpatients in the cohort.

based on medical history, requiring that the patient exhibited both motor and vocal tics over a period of 1 year and that disease onset occurred before the age of 18 without attribution to other disease or substance abuse.<sup>5</sup> Patients may undergo imaging evaluations, but no specific laboratory assays are presently used for the diagnosis of TS. Consequently, TS is frequently underdiagnosed and undertreated, and patients are likely to experience peer rejection or social discrimination that may lead to depression and anxiety.<sup>6,7</sup>

The frequent comorbidities observed in patients with TS included attention-deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder, learning disabilities and autism.<sup>5</sup> Assessments and profiling for comorbid neuropsychological comorbidities are recommended for patients with TS.<sup>5,8</sup> ADHD and learning disabilities worsen the psychosocial health of patients with TS, requiring specialised care or counselling.<sup>5</sup> Nail biting is another behavioural disorder often observed in patients with TS.<sup>9</sup> Nail biting itself affects more than a third of the general population, and its onset predominantly occurs during childhood or adolescence.<sup>10,11</sup> Excessive nail biting can result

in splinter haemorrhage, scarred nail folds, paronychia and even irreversible distortion of the nail beds.<sup>10 12</sup> The association between nail biting and psychiatric conditions such as depression, anxiety and obsessive-compulsive disorder has attracted much attention.<sup>10 12</sup>

Despite the correlation between nail biting and psychological problems, the prevalence and temporal course of this behaviour has rarely been studied in individuals with TS. This retrospective observational study aims to assess and compare the prevalence of nail biting in outpatients at a single institution between those with provisional tic syndrome, TS and controls. The chronological relationship between nail biting and tic development over the course of TS and its association with ADHD are also explored.

## METHODS

### Design and participants

In this retrospective observational study, outpatients aged 4–18 years were recruited from the Department of Pediatrics at the Landseed International Hospital, Taiwan. Outpatients diagnosed with TS from 2015 to 2020 were initially screened for eligibility. Outpatients diagnosed with provisional tic disorder and controls were selected from 2015 to 2016. The diagnostic criteria for TS were as follows: (1) exhibiting both motor and vocal tics for more than 1 year, (2) onset of tics before age 18 and (3) tics not attributed to another medical condition or substance abuse. Provisional tic disorder was defined as the exhibition of motor and or vocal tics for less than 1 year, and diagnosis was based on clinical observations and the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) definition. ADHD was diagnosed based on the Swanson, Nolan and Pelham (IV) Rating Scale. The DSM-5 classifies excessive nail biting as ‘body-focused repetitive behaviour disorder’ under ‘other specified obsessive compulsive and related disorders’. Nail biting behaviour was assessed by the first author, who routinely assesses nail biting problems in all of his patients by questioning the parents/guardians about such behaviour. Outpatients at the same hospital with no neurological or psychiatric disorders were chosen as controls. Patients with autism, cerebral palsy or mental retardation were excluded from the study.

### Study variables

Patient age, sex, presence of nail biting, starting age for nail biting and starting age for motor and/or vocal tics were extracted from medical records. The presence of nail biting, starting age for nail biting and starting age for motor and/or vocal tics were documented according to the memory and description by parents/guardians.

### Statistical analysis

The average age of each group of participants (controls, provisional tic disorder and TS) is expressed as the mean±SD and analysed by one-way analysis of variance

(ANOVA) with Bonferroni adjustment. The age of onset of nail biting and tics is expressed as the mean±SD. Data regarding categorical variables are presented as n (%). Differences between patients with TS with and without ADHD were examined using the two-sample t test for continuous variables and the Pearson  $\chi^2$  test or Fisher’s exact test for categorical variables. The difference in starting age between nail biting and tics in the same patients was examined using the paired t test. The frequency distribution of participants with and without nail biting among control, provisional tic disorder and TS groups is presented as % of cases in bar graph, and the differences in frequency between groups were assessed using  $\chi^2$  or Fisher’s exact test.

The interval between the starting age for nail biting and starting age for tics was calculated as the starting age for nail biting minus the starting age for tics. The intervals between the two events (<0, =0 and >0) indicate that the starting age for nail biting was earlier than, similar to, and later than the starting age for tics, respectively. These intervals in patients with TS with or without ADHD were stratified by age and sex and are presented in box plots. Differences in mean intervals between patients with TS with and without ADHD were evaluated using the Mann-Whitney U test. The prevalence of nail biting was compared between disease groups by adjusting for covariates using multivariate logistic regression analysis. Proportional odds logistic regression analysis was used to examine differences in starting age for tics and nail biting between patients with TS with and without ADHD, with age adjustment. All statistical assessments were two tailed and considered for  $p<0.05$ . All statistical analyses were carried out using IBM SPSS statistical software V.22 for Windows (IBM, Armonk, New York).

### Patient and public involvement

None.

## RESULTS

A total of 3302 children and adolescents were initially reviewed for eligibility retrospectively. Of these, 763 were excluded due to missing age ( $n=1$ ), age  $\leq 3$  years ( $n=1072$ ), age  $>18$  years ( $n=3$ ) and no record indicating the presence or absence of ADHD in patient with TS ( $n=1$ ). As a result, 2225 participants (1397 boys and 828 girls) were included for the final statistical analysis.

Study participants were divided into three groups: controls ( $n=1460$ ), provisional tic disorder ( $n=230$ ) and TS ( $n=535$ ) (table 1). The majority of patients diagnosed with provisional tic disorder and TS were men (75.2% and 83.0%, respectively), and 53.4% of controls were men. Patients with TS had the highest mean age. After stratification by age, the majority of provisional tic disorder and patients with TS aged 7–12 (50.4% and 74.6%, respectively), whereas most of the controls were aged 4–6 years (50.5%) (table 1).

**Table 1** Age distribution of the overall study population and stratified by sex

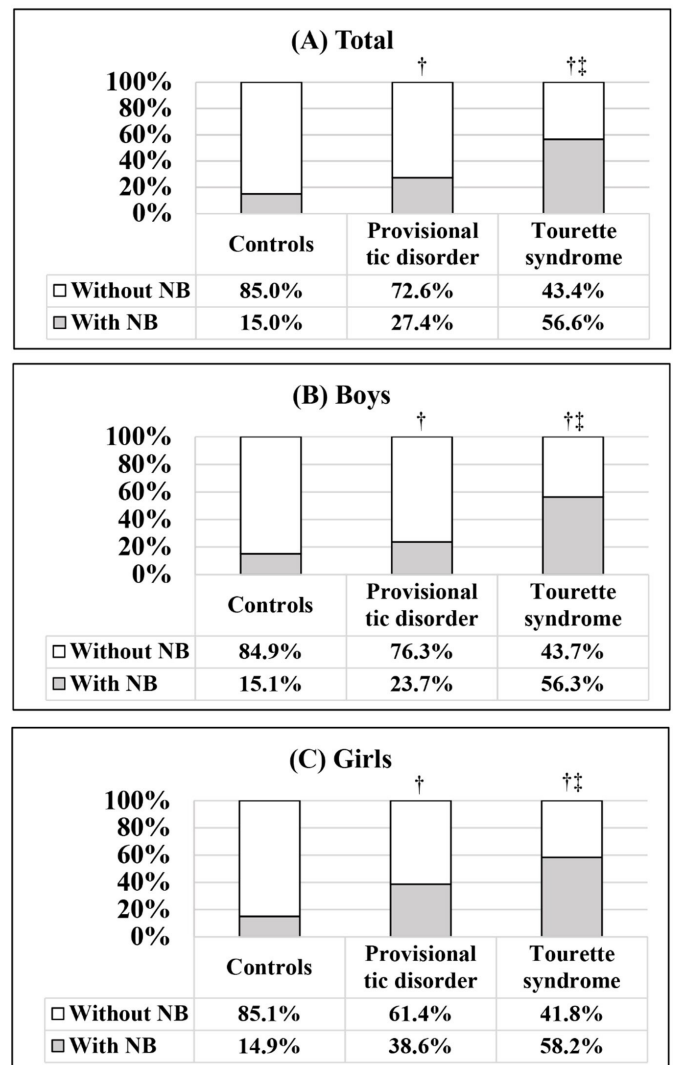
	Controls	Provisional tic disorder	Tourette syndrome	P
<b>Total</b>				
n	1460	230	535	
Age, years (mean±SD)	7.4±3.2	7.0±2.3	9.4±2.8†*	<0.001‡
4–6 years	737 (50.5)	108 (47.0)	68 (12.7)	
7–12 years	575 (39.4)	116 (50.4)	399 (74.6)	
13–15 years	135 (9.2)	5 (2.2)	49 (9.2)	
16–18 years	13 (0.9)	1 (0.4)	19 (3.6)	
<b>Boys</b>				
n	780	173	444	
Age, years (mean±SD)	7.3±3.1	7.0±2.3	9.5±2.8†*	<0.001‡
4–6 years	384 (49.2)	83 (48.0)	52 (11.7)	
7–12 years	325 (41.7)	85 (49.1)	334 (75.2)	
13–15 years	67 (8.6)	5 (2.9)	41 (9.2)	
16–18 years	4 (0.5)	0 (0)	17 (3.8)	
<b>Girls</b>				
n	680	57	91	
Age, years, (mean±SD)	7.4±3.3	7.1±2.3	8.9±2.8†*	<0.001‡
4–6 years	353 (51.9)	25 (43.9)	16 (17.6)	
7–12 years	250 (36.8)	31 (54.4)	65 (71.4)	
13–15 years	68 (10.0)	0 (0)	8 (8.8)	
16–18 years	9 (1.3)	1 (1.8)	2 (2.2)	

Data are presented as n (%) for each age group.  
 \*Statistically significant compared to controls.  
 †Statistically significant compared to the provisional tic disorder group.  
 ‡Indicates significant difference between the three groups.

The prevalence of nail biting in the three groups is shown in [figure 1](#). The frequency of nail biting was significantly higher among patients with TS (56.6%) than those with provisional tic disorder (27.4%) and controls (15.0%) ([figure 1A](#)). Since the average age was higher in the TS group, age was considered as an important covariate and was adjusted in logistic regression models. The results showed that the frequency of nail biting was higher in patients with provisional tic disorder and/or TS after adjustment for age (all  $p < 0.001$ ) (online supplemental table S1). After stratifying by sex, boys and girls with TS also had the highest frequency of nail biting (56.3% and 58.2%, respectively), compared with their counterparts with provisional tic disorder and controls (all  $p < 0.010$  after adjustment for age) ([figure 1B and C](#)).

Within the TS group, 176 patients also had ADHD (157 boys (89.2%) and 19 girls (10.8%)) ([table 2](#)). Boys with TS had a significantly higher prevalence of ADHD than did their girl counterparts ( $p = 0.008$ ). Overall, patients with concomitant TS and ADHD had a significantly higher prevalence of nail biting than did patients with TS alone, regardless of sex (all  $p \leq 0.002$ ). Patients with concomitant TS and ADHD had a significantly higher starting age for nail biting than did those with TS alone, with or without stratification by sex (total population and boys,  $p < 0.001$ ; girls,  $p = 0.023$ ). In contrast, a significant difference in

Figure 1



**Figure 1** The prevalence of nail biting among the controls and patients with provisional tic disorder or Tourette syndrome among (A) the total study population, (B) boys and (C) girls. NB, nail biting. ††Significant difference compared with controls† and temporary tics† (all  $p < 0.020$ ).

starting age for tics between patients with TS with and without ADHD was observed only in the total population and boys ( $p = 0.007$  and  $p = 0.008$ , respectively). The starting age for nail biting was significantly earlier than that for tics in the overall and male patients with TS with or without concomitant ADHD and in female patients with concomitant TS and ADHD (all  $p < 0.001$ ). As such, the majority of patients with TS started nail biting before the onset of tics, regardless of ADHD or sex ([table 2](#)).

In the total population, patients with TS alone had a significantly lower interval between the age of onset of nail biting and tics than did those with both TS and ADHD in the age groups of 7–12 years and 13–15 years ( $p = 0.040$  and  $0.017$ , respectively) ([figure 2](#)). The mean interval between the age of onset of nail biting and tics was  $-2.14$  for boys with TS and  $-1.71$  years for girls with TS, with no significant sex-specific difference ( $p > 0.05$ ,

**Table 2** Age of onset for nail biting and tics among patients with Tourette syndrome

	All patients with TS		Boys with TS		Girls with TS		P	
	ADHD	Non-ADHD	ADHD	Non-ADHD	ADHD	Non-ADHD		
n	176	359	157	287	19	72		
Sex	0.008*							
Boys	157 (89.2)	287 (79.9)						
Girls	19 (10.8)	72 (20.1)						
Age	0.109							
4–6 years	15 (8.5)	53 (14.8)	12 (7.6)	40 (13.9)	3 (15.8)	13 (18.1)		
7–12 years	143 (81.3)	256 (71.3)	128 (81.5)	206 (71.8)	15 (78.9)	50 (69.4)		
13–15 years	12 (6.8)	37 (10.3)	11 (7.0)	30 (10.5)	1 (5.3)	7 (9.7)		
16–18 years	6 (3.4)	13 (3.6)	6 (3.8)	11 (3.8)	0 (0)	2 (2.8)		
Nail biting	< 0.001*							
With	132 (75.0)	171 (47.6)	115 (73.2)	135 (47.0)	17 (89.5)	36 (50.0)		
Without	44 (25.0)	188 (52.4)	42 (26.8)	152 (53.0)	2 (10.5)	36 (50.0)		
Starting age for nail biting	5.3±2.5†	3.8±3.0†	5.3±2.6†	3.8±3.0†	5.3±1.9	3.6±2.9†	0.023*	
Starting age for tics	6.6±1.8	6.2±2.0	6.7±1.8	6.3±2.0	5.8±1.7	5.8±2.0	0.891	
Sequence of nail biting	0.902							
Same as tics	31 (23.5)	38 (22.4)	27 (23.5)	30 (22.4)	4 (23.5)	8 (22.2)		
Before tics	75 (56.8)	95 (55.9)	68 (59.1)	76 (56.7)	7 (41.2)	19 (52.8)		
After tics	26 (19.7)	37 (21.8)	20 (17.4)	28 (20.9)	6 (35.3)	9 (25.0)		

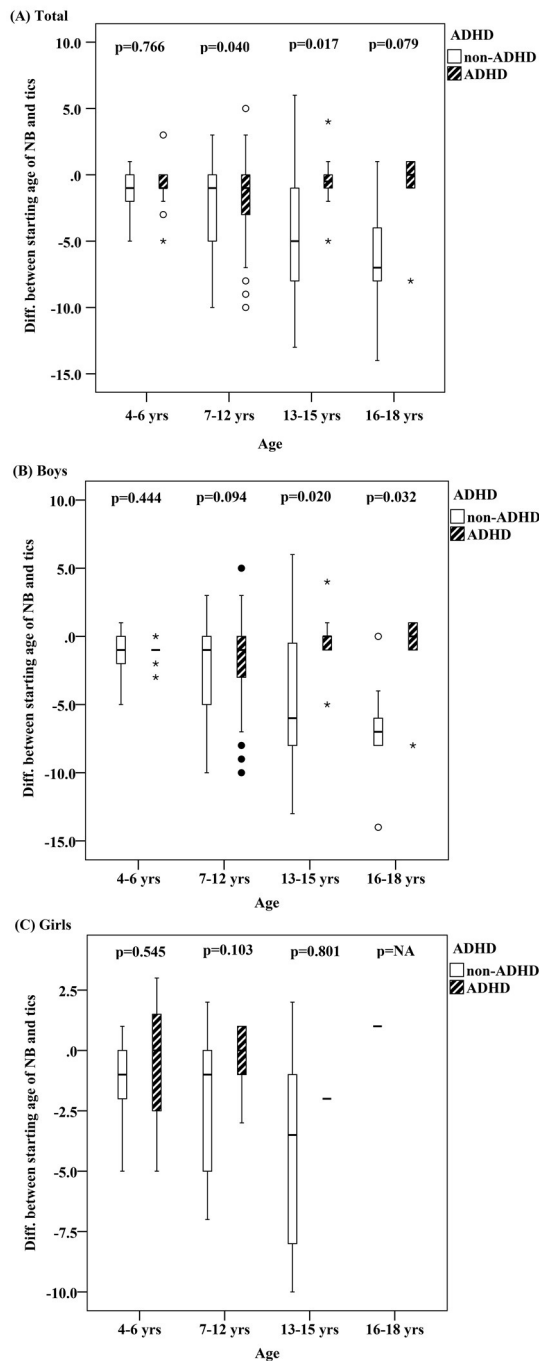
Data are expressed as n (%) for age, sex and nail biting.

\*Significant difference between ADHD and non-ADHD.

†Significant compared with starting age of tics as tested by proportional odds ordinal logistic regression models. ADHD, attention deficit hyperactivity disorder; TS, Tourette syndrome.;



Figure 2



**Figure 2** Time difference between tic onset and nail biting onset in Tourette syndrome patients with and without ADHD, stratified by age, among (A) the total study population, (B) boys and (C) girls. ADHD, attention deficit/hyperactivity disorder; NB, nail biting; Yrs, years.

data not shown). After further stratification by the presence of ADHD, boys with concomitant TS and ADHD had a significantly shorter mean interval between the two events than did boys with TS alone ( $-1.4$  vs  $-2.6$ ;  $p=0.006$ ; data not shown). Girls with concomitant TS and ADHD also had a shorter interval between the two events than did girls with TS alone, but the difference did not reach

statistical significance ( $-0.6$  vs  $-2.1$ ;  $p=0.084$ ; data not shown).

Stratification by age subgroups showed that boys with TS alone had a significantly lower interval between the two events than sis boys with both TS and ADHD in the age groups of 13–15 and 16–18 years ( $p=0.020$  and  $0.032$ , respectively) (figure 2B). However, no significant difference in the interval was observed between TS girls with and without ADHD for any age group studied (figure 2C). In addition, the interval between the two events decreased with age in boys with TS alone but remained relatively steady among all age groups in boys with both TS and ADHD (figure 2B). A similar decreasing trend in the interval between the two events was observed in girls with TS alone across all age groups (figure 2C).

## DISCUSSION

Although nail biting and tics are common in children with mental and psychological illnesses, including TS, the relationship between tics and nail biting is rarely investigated. In the present study, we evaluated the prevalence of nail biting among TS hospital outpatients at a single centre and explored the chronological relationship of nail biting and tic onset in these patients over the course of the disease and how this relationship was affected by concomitant ADHD. We found that the prevalence of nail biting was significantly higher in the TS group than in controls and patients with provisional tic disorder. Among patients with TS, the prevalence of nail biting was significantly higher in those with concomitant ADHD than in those without. The mean starting age for tics was overall similar across the different TS subgroups, but the mean starting age for nail biting was significantly later in patients with concomitant TS and ADHD than in those with TS alone. While the mean starting age for nail biting was significantly earlier than that for tics in patients with TS with and without ADHD, the time interval between the onset of nail biting and the onset of tics was significantly greater in patients with TS alone than in those with concomitant TS and ADHD. The difference in this time interval between patients with TS with and without ADHD tended to increase with age and reached statistical significance in the age groups of 13–15 and 16–18 years for boys and 7–12 years for girls.

Patients with TS often develop comorbid mental and psychological illnesses,<sup>9</sup> which may contribute to the underdiagnosis and undertreatment of TS. Timely diagnosis and pharmacological or behavioural intervention is critical for a young patient's psychosocial development and quality of life in subsequent years.<sup>13 14</sup> With no specific laboratory test for diagnosing TS, the criteria for diagnosis focus heavily on the recall/observation of tic symptoms and the absence of other aetiologies. The Yale Global Tic Severity Scale (YGTSS), commonly used to assess tic disorder and TS severity, was shown to be a promising tool with good discriminative ability in Taiwanese children.<sup>15</sup> The YGTSS combines the

observations of a health professional and patient/family, so that adequate patient/family awareness and user experience may be required for accurate assessment.<sup>15</sup> Some children may present tics that eventually resolve within 1 year, resulting in a distinct diagnosis of provisional tic disorder rather than TS.<sup>4</sup> All of these issues encountered in actual clinical practice may hinder TS diagnosis and treatment.

Present treatments for tics in TS and other chronic tic disorders commonly involve behaviour and/or pharmacological therapies, with behaviour prioritised before pharmacological treatments.<sup>16</sup> For those who do not successfully respond to behavioural therapy, a variety of pharmacological agents or alternative therapies such as deep brain stimulation and cannabis-based medicine may be considered.<sup>16</sup> A recent systematic review strongly supports the use of Comprehensive Behavioral Intervention for Tics (CBIT) over supportive psychotherapy alone.<sup>17</sup> CBIT usually involves habit reversal training, psychoeducation on tics, function-based interventions and relaxation training delivered in eight sessions over a 10-week period. However, in settings where qualified behavioural therapists are limited, the standard of care remains supportive counselling and psychoeducation.<sup>14</sup> A recent randomised clinical trial conducted in Taiwan compared the effectiveness of local routine care (daily pyridoxine plus psychoeducation) alone or combined with a modified CBIT consisting four behavioural intervention sessions in a 3-month programme, and the modified CBIT was shown to significantly decrease the severity of tics and YGTSS scores compared with routine care.<sup>14</sup> Children affected by concomitant TS and ADHD may require additional care and treatment than those with TS alone.<sup>18</sup>

The prevalence of nail biting and ADHD among 35 Iranian children with TS was reported as 28.6% and 68.6%, respectively, in a retrospective review.<sup>9</sup> However, the study did not include controls or patients with provisional tic disorder, and the association between nail biting and ADHD within the context of TS was unexplored. Another study showed that among children displaying a nail biting habit, the prevalence of ADHD was 74.6% and tic disorder was 12.7%.<sup>19</sup> Interestingly, a postdiagnosis survey conducted in 53 patients with TS aged 13–31 years found that the tics and ADHD onsets were extremely close to each other, as was the remission of both symptoms.<sup>20</sup>

Although we found a significant difference in the onset age for nail biting between young TS individuals with and without ADHD, the underlying pathogenesis and clinical application of this finding are beyond the scope of our study. Nevertheless, these observations suggest that developmental differences potentially attributable to hormonal or neurophysiological factors may be at play in the two TS subgroups. Familial, psychiatric and behavioural factors are reported to be associated with paediatric nail biting, with an onset around 5 years of age.<sup>21</sup> A closer inspection of children's behaviour should be considered when the nail biting habit appears around the beginning of school

age, as it may be confused with anxiety associated with a new learning environment.

In spite of the consistency of the findings presented here, this study is limited by several intrinsic caveats. The study design is retrospective in nature and the cohort only included patients at a single institute in Taiwan, all of whom were hospital outpatients. In addition, the number of girls with TS in the cohort were small, particularly for those  $\geq 13$  years of age. Thus, the results need to be confirmed by a large-scale study conducted in different geographical areas or ethnic groups. Prospective enrolment may be used in the future studies to minimise the potential confounding of results by patient symptom recall.

## Conclusion

This single-centre, retrospective, observational study indicates that nail biting appears to be a more predominant behavioural feature among patients with TS, especially those with comorbid ADHD, than in controls and patients with provisional tic disorder. The onset age for nail biting was consistently earlier than that for tics in patients with TS, regardless of comorbid ADHD and sex. Paradoxically, the time interval between starting age for nail biting and starting age for tics was lower in patients with concomitant TS and ADHD than in those with TS alone. These findings highlight the potential differences in disease progression between patients with concomitant TS and ADHD than those with TS alone. Our preliminary findings suggest that further research may provide insights into the disease course of concomitant TS and ADHD.

**Contributors** C-WH: conception and design, analysis and interpretation of data, critical revision of the manuscript, responsible for the overall content as the guarantor; C-WC: acquisition of data, drafting of the manuscript. All authors have read and approved the final version of the manuscript.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** This study protocol was approved by the Institutional Review Board (IRB Number 18-008-B1) of the Landseed International Hospital, and the requirement for informed consent was waived by the same IRB because of the retrospective nature of this study. This study was performed in line with the principles of the Declaration of Helsinki.

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