# Clinical Factors Associated with PANDAS

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## Abstract

**Objective**—To explore associated clinical factors in children with pediatric autoimmune neuropsychiatric disorders associated with streptococcus (PANDAS).

**Study design**—Children with tics and/or OCD (*n* = 109) were examined by personal and family history, diagnostic interview, physical examination, medical record review, and measurement of baseline levels of streptococcal antibodies.

**Results**—Significant group differences were found on several variables, such that those diagnosed with PANDAS (versus without PANDAS) were more likely to have had dramatic onset; definite remissions; remission of neuropsychiatric symptoms during antibiotic therapy; a history of tonsillectomies/adenoidectomies; evidence of GAS infection, and clumsiness.

**Conclusion**—The identification of clinical features associated with PANDAS should assist in delineating risks for this subtype of OCD/tics.

## Keywords

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections; PANDAS; Obsessive-Compulsive Disorder; Tic disorder; Children

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The term PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections) refers to a disorder in children who manifest symptoms of obsessive-compulsive disorder (OCD) and/or tic disorders associated with a distinctive course, a temporal association with group A streptococcal (GAS) infection, and evidence of concurrent neurologic abnormalities (i.e., severe hyperactivity, fine motor skill loss [handwriting deterioration] or adventitious movements such as choreiform movements) (1). The distinctive course is defined by prepubertal onset of symptoms, episodic symptom severity, and a range of other psychiatric symptoms (e.g., irritability, frequent mood changes, separation anxiety, hyperactivity, late onset attention problems, personality change,

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oppositional behaviors) as well as sleep disturbances and deterioration in math skills and handwriting (2, 3).

Distinguishing PANDAS from other presentations of OCD or tics and, occasionally, from Sydenham chorea (SC) confounds researchers and clinicians, making it difficult to establish practical treatment protocols. Currently, careful delineation of the neuropsychiatric course offers the best framework with which to study the proposed GAS association. A core feature of PANDAS has been a dramatic onset and a fluctuating course, with course characteristics (e.g., episodic, sawtooth, remitting, progressing, chronic) likely varying with age of onset, illness duration, pattern of comorbidity, and the patient's sex. Although both tic and obsessive compulsive disorders have the potential to manifest a chronic and disabling course, only tic disorder nosology acknowledges the potential for an episodic course. Perhaps less recognized, OCD often has an episodic course (4) with some individuals spontaneously remitting (5). Whether those presenting with a PANDAS subtype typically will go on to remission or progress to a more chronic course of illness is not known. In other words, the symptom course that is characteristic of PANDAS may not differ from the typical course of OCD and tics early in the illness.

With the exception of children with an explosive onset of OCD/tics occurring simultaneously with GAS, the timing and the type of GAS association to make a definitive argument for PANDAS has not been well defined. The main issue is the differentiation of a true inciting GAS infection, whether clinical or subclinical, from GAS carrier states. Even further uncertainty exists regarding how much importance to ascribe to GAS exposure from close contacts. How synchronous the temporal association between GAS infection (or exposure) and symptom onset has thus far been undefined. It has been proposed that neuropsychiatric symptom onset that occurs one to six months after GAS infection could be a chance association (6). However, in cases of pure SC (no evidence of carditis), an infection triggered etiology generally is presumed by the presence of GAS antibody elevations that can be observed after a time lag between the suspected inciting infection and the onset of symptoms. GAS antibody elevations observed within weeks of the onset of OCD or tics is not enough in the current state of the field to establish a diagnosis of PANDAS.

Unfortunately, PANDAS criteria and associated clinical features that may serve to differentiate PANDAS from OCD/tics disorders without PANDAS are not well established. The purpose of this study was to examine which core features of PANDAS (e.g., OCD/tic symptom course, GAS infection history, neurologic symptoms, and immune history) provide the most meaningful differentiation between subjects with and without a PANDAS classification, as well as which additional clinical factors best exemplify the PANDAS presentation in order to advance the understanding of risks related to disease onset.

## METHOD

One hundred and nine patients with childhood onset OCD and/or tics ages 4–17 years were asked to participate in the study. The study inclusion criterion was meeting the DSM-IV criteria for OCD and/or a tic disorder. Recruitment was weighted to enrolling children with history of any infection-related symptom flare-ups *or* history of dramatic onset of either OCD or tics, although children not meeting these criteria also were included. Age of symptom onset was determined using all available information including pediatrician records as well as reports from parents and teachers and self-reports from the child. Patients with a psychotic disorder, significant medical illness, or non-tic neurologic disorder at baseline were excluded from the study. Patients on stable doses of psychotropic medication for their condition were not excluded.

### Measures

The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime (K-SADS-P (7)) is a structured clinical interview to assess the presence of DSM-IV diagnoses in children. The Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS (8)) is a clinician-rated, semi-structured interview that assesses the severity of OCD symptoms; strong psychometric properties have been demonstrated. The Yale Global Tic Severity Scale (YGTSS (9)) is a clinician-rated, semi-structured interview that assesses tic severity; strong psychometric properties have been documented.

A filmed neurologic examination was conducted to record any adventitious facial and limb movements, spooning or extension of arms, or other movements based on both the neurologic examination of soft signs (10) and the choreiform movement assessment (11). Videotapes were scored by an experienced rater (PJE) blinded to subjects' clinical and serologic status. In the choreiform segment, subjects were assessed with arms/hands outstretched in pronated and supinated positions (20 seconds each), then rated for severity of distal (fingers and wrist) and proximal (arms, elbows and shoulders) choreiform (quick, jerky) movements. Movements were scored using Touwen 0–3 scale: 0 = no movement visible during the 20 seconds; 1 = 2–5 isolated twitches; 2 = 6–10 twitches; 3 = continuous twitching (11).

The Immune-Related OCD/TS Evaluation (I-ROTE), an evaluation tool devised by the first author, was completed by the physician with the parent of each subject. The use of this instrument with patients assumes a diagnosis of OCD or tics. The I-ROTE elicited information germane to the diagnosis of immunologic conditions, infections, rheumatic fever, SC and other movement disorders. Detailed descriptions regarding course of neuropsychiatric symptoms were obtained as well as examination of the presence of PANDAS operational criteria developed by Swedo (3), age of symptom onset of symptoms, symptom characteristics and parental impression of symptom course. This instrument also screened for family history of autoimmune illnesses, recent stresses, and impact of medications on illness course.

### Study Procedures

This study was approved by the institution's human subjects review board. Study procedures were explained, the informed consent was reviewed and parents/subjects were given the opportunity to ask questions. Prior to participation, parents gave written consent and subjects gave oral assent as well as, where age-appropriate (≥ 7 years), written assent. Following, subjects participated in the baseline assessment using the measures reviewed above. All assessments were conducted either by the first author or by a trained clinician with experience in pediatric OCD and tic disorders. Ratings were based upon patient and parent response, clinician judgment, and behavioral observation.

**Case Assignment—**Participant diagnostic information, symptoms, and family history of autoimmune disorders were obtained through clinical interview; medical records; baseline laboratory tests, including streptococcal antibodies; and psychological ratings. Specific areas of interest were the following: participant diagnosis of immunologic conditions, infections, rheumatic fever, SC and other movement disorders; course of neuropsychiatric symptoms; age of symptom onset; details regarding comorbid presentations; extent of GAS infection and exposure, other infectious triggers; recent stresses; and presence of PANDAS operational criteria as developed by Swedo et al (3). For each participant, the first author assigned a classification of either 'PANDAS' or 'without PANDAS' (course and GAS relatedness not consistent with PANDAS) based on putative criteria described by Swedo et al. To establish inter-rater reliability of the caseness rating, the third author independently

assessed a subsample of 25 cases. Assessment consisted of a review of all available data. Overall, inter-rater reliability was high (intraclass correlation coefficient = 0.86). These data were designed to assimilate an impression of PANDAS at an initial presentation during a clinical assessment by the child's pediatrician or psychiatrist without any prospective observation.

**Streptococcal antibodies—**Three antibody assays (antistreptolysin O (ASO), anti-deoxyribonuclease B (anti-DNAseB) and anti-A carbohydrate (anti-$A_{CHO}$)) were collected on 99 of the 109 children. The use of three antibodies reduces the false negative rate of a single test from 20% to about 5–10%. All streptococcal antibody tests were performed in the University of Florida's streptococcal antibody laboratory. To minimize assay variability and to maximize the ability to detect individual's changes over time, the full complement of samples from the same patient was assayed in the same run. The Sure-Vue ASO test kit (12) was used. Reagents used, technique, reading and interpretation of the anti-DNase B and anti-$A_{CHO}$ assays have been described previously (13).

Previous studies have established that a significant antibody rise can be detected about two weeks after an acute streptococcal infection (i.e., pharyngitis) and that the antibody response typically peaks 3 to 4 weeks after that infection (14). A child was classified as having elevated titers if any one of the three levels obtained at the baseline visit was above the set threshold. Thresholds used were ≥200 for ASO, ≥240 for the DNASeB and ≥2.76 for the anti-$A_{CHO}$ antibody levels. These levels were not age adjusted and may have resulted in some false-negative results for children in the preschool range (15).

### Analytic Design

Descriptive statistics were calculated for study variables. Group differences (in PANDAS caseness) were examined using Chi-square; risk ratios were calculated to report likelihood of subjects with PANDAS to present with a particular criterion. No statistical correction for multiple tests was used.

## RESULTS

One hundred and nine patients (66.6% males) were asked to participate in the study. Average age was $9.2 \pm 2.4$ years; average age of onset of disorder was $5.7 \pm 2.5$ years. Demographic data are presented in Table I. Of the 109 subjects, 41 were classified as having PANDAS (28 male; mean age at evaluation = 8.63 years, SD = 2.1). Those without PANDAS (N = 68) had a mean age of 9.36 (SD = 2.3) and 38 were male. Those in the PANDAS group were statistically more likely to: (1) have had definite remissions in neuropsychiatric symptoms; (2) have dramatic onset of symptoms; (3) have definite remissions; (4) show remissions of neuropsychiatric symptoms during antibiotic therapy; (5) have elevated streptococcal titers; (6) have episodes of fever/sore throat at onset/flare up; (7) show positive GAS culture with symptom onset/flare up; and (8) present with clumsiness. Risk ratios and inferential statistics are presented in Table II. Duration of illness was shorter in those classified as PANDAS. No notable group differences were found in affective instability, episodic psychotic symptoms, OCD, tic disorder or separation anxiety. Although not statistically significant, 61% of PANDAS subjects had ADHD versus 46% of those without PANDAS. An elevation of one or more streptococcal titers was found in all the subjects with PANDAS (by case definition), especially ASO antibody (Table III). Using stringent criteria for GAS association (documented GAS culture or rising antibodies) at onset or flare up with course features that included dramatic onset and definite remissions, 46% of the PANDAS group met this requirement versus 10% in the without PANDAS group. The remaining 54% of those with PANDAS had dramatic onset with GAS (n=15),

GAS exposure (n=2), or fever (n=5). Documentation of rise in ASO and anti-DNAse-B antibodies between time of onset to 4–8 weeks later was found in only a minority of subjects (based on previously obtained clinical studies prior to baseline assessment).

## DISCUSSION

The present study set out to determine the strength of core and associated clinical factors with PANDAS caseness. Although limitations of the study included the subjective assessment of raters based on original features of PANDAS and the accuracy of recall of symptoms and onset by parents, significant study strengths include the use of objective laboratory values and extensive review of factual medical records. As defined by the putative PANDAS criteria and supported by the clinician's impression of PANDAS caseness, GAS correlation, dramatic onset, definite remission were strong predictors. Although nearly all of our subjects were prepubertal at symptom onset, those having a shorter duration of illness were more often associated with a PANDAS presentation. One possibility is that patients evaluated earlier in their course of illness have a higher reporting of GAS association and are more likely to have an episodic course with more definitive remissions. Whether this observation is related to the etiology of onset or is a clinical coincidence will need further investigation.

We did not find specificity for some characteristics thought to distinguish PANDAS, namely dramatic flare-ups and choreiform movements. Another observation that was more specific to the PANDAS group was remission or partial remission of symptoms while on antibiotics. The design of the two published studies has precluded drawing a definitive conclusion on the efficacy of antibiotic use for PANDAS (16–19). The safety, efficacy, dosing and duration of antibiotic use for purported cases of PANDAS needs further study before recommendation.

At least one streptococcal antibody was elevated in most patients regardless of group assignment. Although many of the patients were recruited into this study because they had some features of PANDAS (i.e., flare-ups, frequent streptococcal infections, etc.), this finding is not surprising. Elevated ASO antibody was the only antibody significantly associated with cases versus non-cases (59% versus 37%, respectively; p=0.03). Streptococcal antibody tests provide evidence only for an antecedent streptococcal infection. It is important to note that elevations in these antibodies are not diagnostic of PANDAS but requires careful consideration of the clinical history and examination. In some cases, particularly for very young children, limited prior exposures to GAS might affect likelihood of surpassing the threshold for elevated antibody levels. Other factors such as hyperlipidemia, treatment with antibiotics, and the individual's ability to mount a strong immune response, are other potential reasons for variations in antibody levels. Frequent exposure, reinfection (20) or stronger than typical immune responses (21) to GAS are likely reasons for sustained titers or the slower rate of decline in some of these children and may contribute to a fluctuating course (5).

An increased rate of OCD and Tourette syndrome in first-degree family members of patients with PANDAS (22) has been reported. In the case series of 54 patients with PANDAS, 39% had family history of tics and 23% had family history of OCD (when subclinical OCD cases were included) in 100 first-degree relatives. Currently, the prevalence of immune disorders in family members has not been examined in the PANDAS subtype of OCD or tics despite some clinical evidence of a linkage (1, 23). Family members of our subjects had a substantial prevalence of autoimmune disease compared with the general population (24).

We found a high association between PANDAS caseness and rate of tonsillectomies and adenoidectomies. This finding may suggest that pre-existing infections such as otitis and pharyngitis were related to risk of developing neuropsychiatric symptoms (25, 26) or that removal of this lymphoid tissue increased immunologic risks (27, 28) that may be associated with increased risk of OCD/TS (5). Although symptomatic GAS infections have been shown to decrease after tonsillectomy (29), the role of non-carrier state subclinical infections has not been documented. Recent research has shown that children with hypertrophy of adenoids and tonsils exhibit both local and general changes in immunologic parameters (27). Both humoral (immunoglobulins A, G, M levels) and cellular (CD3+, CD4+, CD8+ lymphocyte counts) immune factors decreased significantly postoperatively, but at six months postoperatively, findings are normal. The impact of a transient, immune modulation associated with surgical removal of the tonsils and/or adenoids on the development of autoimmune sequelae has not been studied.

Approximately one-half of all of our subjects had multiple streptococcal infections prior to the age of 7 years (49% of group overall, 56% of those with PANDAS). Recent studies (3, 10, 30) suggest risk associated with repeat GAS infections in children who have neuropsychiatric symptoms. For example, a history of multiple GAS infections within a 12-month period was associated with increased risk for Tourette syndrome (OR = 13.6; 36). Another source found number of prior GAS infections to be positively related to severity of course and incidence of relapse (3). A school study examining motoric signs and behavior while obtaining monthly GAS cultures on 693 schoolchildren found that those with repeated GAS infections during the 8-month study had more frequent neuropsychiatric findings (25). In our study, we were specifically interested in those with frequent GAS infections at an early age. Vulnerability to neuropsychiatric sequelae may occur when a cumulative threshold effect of repeat infections is reached in a young child. Although development of rheumatic fever (RF) is rare in children under five years, the impact of early GAS infections on future immune response to GAS and neuropsychiatric vulnerability is unknown. Neuroimmune reactions may be non-specific to the type of infectious trigger and secondary to an inherent, broader immunologic risk. Reasons for GAS recurrence are likely complex and numerous (31). Most of the recurrences of GAS are relapses (ie, infection by the same streptococcal strain rather than new infections due to a different strain) (20).

Currently, the exact prevalence of the PANDAS subtype remains unknown (32), as most studies of PANDAS have been based on targeted recruitment, leading to difficulties in identification of base-rates and probabilities for encountering the disorder. For example, even though all our subjects had OCD and/or tics, our study selected for subjects who met two or more PANDAS criteria (i.e., prepubertal onset, fluctuating course, dramatic onset, GAS association). Most subjects were prepubertal and many had a fluctuating course but only a minority met more stringent criteria for PANDAS requiring dramatic onset and clearly identifiable association with GAS. Notably, despite our attempt from the outset to enrich the sample with PANDAS, only 38% were assigned the PANDAS classification. The current study advances the literature by validating a set of largely objective criteria relative to clinician impression. Defining risks and associated features will have a major impact on determining the etiology of this pediatric disorder and evaluating treatments.

## Acknowledgments

## Abbreviations

| | |
|---|---|
| **PANDAS** | Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections |
| **OCD** | Obsessive-Compulsive Disorder |
| **GAS** | Group A Streptococcal |
| **SC** | Sydenham chorea |
| **RF** | rheumatic fever |
| **NSS** | neurological soft signs |
| **K-SAD-PL** | Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime |
| **CY-BOCS** | Children's Yale-Brown Obsessive Compulsive Scale |
| **YGTSS** | Yale Global Tic Severity Scale |
| **I-ROTE** | Immune-Related OCD/TS Evaluation |
| **ADHD** | Attention-Deficient Hyperactivity Disorder, ASO, anti-streptolysin O |
| **anti-A$_{CHO}$** | anti-DNaseB (anti-deoxyribonuclease B, anti-group A streptococcal carbohydrate antigen |

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**Table 1**

Subject Demographics by Group Classification

| | PANDAS | | | Without PANDAS | | |
|---|---|---|---|---|---|---|
| | Total (%) | M (%) | F (%) | Total (%) | M(%) | F (%) |
| **Subjects enrolled** | 41 | 28 (68) | 13 (32) | 68 | 38 (56) | 30 (44) |
| **Ethnicity** | | | | | | |
| *Hispanic* | 2 (5) | 2 (7) | 0 | 5 (7) | 4 (10) | 1 (3) |
| *Asian* | 0 | 0 | 0 | 3 (4) | 3 (8) | 0 |
| *African American* | 1 (2) | 1 (4) | 0 | 0 | 0 | 0 |
| *Caucasian* | 38 (93) | 25 (89) | 13 (100) | 60 (88) | 31 (82) | 29 (97) |
| **Diagnosis** | | | | | | |
| *OCD, no tics (n=22)* | 8 (20) | 5 (18) | 3 (23) | 14 (21) | 4 (11) | 10 (33) |
| *Tic; no OCD (n=19)* | 5 (12) | 3 (11) | 2 (15) | 14 (21) | 10 (26) | 4 (13) |
| *OCD + Tic (n=68)* | 28 (68) | 20 (71) | 8 (62) | 40 (59) | 24 (63) | 16 (53) |
| *ADHD (n=56)* | 25 (61) | 18 (64) | 7 (54) | 31 (46) | 20 (53) | 11 (37) |
| *Affective Instability* | 24 (59) | 15 (54) | 9 (69) | 42 (62) | 24 (63) | 18 (60) |
| *Psychotic Symptoms* | 5 (12) | 4 (14) | 1 (8) | 6 (9) | 3 (8) | 3 (10) |
| *Separation Anxiety* | 12 (29) | 8 (29) | 4 (31) | 15 (22) | 7 (18) | 8 (27) |
| **Duration of illness (yrs)** [*] | 2.8 | 2.8 | 2.7 | 3.9 | 3.8 | 4.0 |
| **Age at onset (yrs)** | 5.9 | 5.8 | 6.1 | 5.6 | 5.8 | 5.5 |
| **Ratings** | | | | | | |
| CYBOCS | 21.8±7.3 | 21.2±7.6 | 22.8±6.7 | 20.6±9.6 | 19.9±10.1 | 21.3±8.9 |
| YGTSS | 21.7±9.9 | 19.56±9.7 | 21.2±10.8 | 17.2±9.9 | 18.2±10.3 | 15.5±9.2 |

[*] Duration of illness was significantly shorter for those youth meeting PANDAS caseness versus those who did not (t(107)=−2.27, p<.025).

**Table 2**

Frequency of symptom item adherence by PANDAS caseness

| | Total (n=109) | | PANDAS (n=41) | | Without PANDAS (n=68) | | PANDAS vs. Without PANDAS | |
|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | Chi² | Risk Ratio |
| Definite prepubertal symptoms | 103 | 94.5 | 40 | 97.6 | 63 | 92.6 | --b | 1.05 |
| Male gender | 66 | 60.6 | 28 | 68.3 | 38 | 55.9 | 1.65 | 1.22 |
| OCD only | 22 | 20.2 | 8 | 19.5 | 14 | 20.6 | .02 | .95 |
| Tic disorders only | 19 | 17.4 | 5 | 12.2 | 14 | 20.6 | 1.25 | .59 |
| OCD and tic disorder | 68 | 62.4 | 28 | 68.3 | 40 | 58.8 | .98 | 1.16 |
| **Diagnosis/Course** | | | | | | | | |
| Definite remissions | 68 | 62.4 | 31 | 75.6 | 37 | 54.4 | 4.90* | 1.39 |
| Dramatic onset | 62 | 56.9 | 29 | 70.7 | 33 | 48.5 | 5.14* | 1.46 |
| Dramatic Flare-ups | 73 | 67.0 | 29 | 70.7 | 44 | 64.7 | .42 | 1.09 |
| Onset new and significant but not dramatic | 28 | 25.7 | 11 | 26.8 | 17 | 25.0 | .04 | 1.07 |
| Dramatic onset + Definite remissions | 40 | 36.7 | 21 | 51.2 | 18 | 26.5 | 6.82* | 1.94 |
| Rising ASO/DNAseB/ACHO titers | 7 | 6.4 | 5 | 12.2 | 2 | 2.9 | --b | 4.15 |
| Elevated ASO/DNAseB/ACHO titers (of 99 with baseline data) | 77 | 77.8 | 39 | 100 | 38 | 63 | 18.4**** | 1.58 |
| Remission of neuropsychiatric symptoms during antibiotic therapy | 17 | 15.6 | 12 | 29.3 | 5 | 7.4 | 9.33** | 3.98 |
| GAS exposure via a family member | 13 | 11.9 | 2 | 4.9 | 11 | 16.2 | --b | .30 |
| **Infection Related** | | | | | | | | |
| Fever and/or clinical sore throat without GAS confirmed | 23 | 21.1 | 5 | 12.2 | 18 | 26.5 | 3.3 | .46 |
| Positive GAS culture | 59 | 54.1 | 32 | 78.0 | 27 | 39.7 | 15.14**** | 1.96 |
| Rising titers O Positive GAS culture R | 62 | 56.9 | 34 | 82.9 | 28 | 41.2 | 18.2**** | 2.01 |
| Frequent GAS infections before 7 years of age | 53 | 48.6 | 23 | 56.1 | 30 | 44.1 | 1.47 | 1.27 |
| History of Tonsillectomies/adenoidectomies | 34 | 31.2 | 19 | 46.3 | 15 | 22.1 | 7.03** | 2.10 |
| Compulsive/frequent urination | 34 | 31.2 | 17 | 41.5 | 17 | 25.0 | 3.23 | 1.66 |
| Handwriting deterioration | 24 | 22.0 | 12 | 29.3 | 12 | 17.6 | 2.01 | 1.66 |
| **Neurologic** | | | | | | | | |
| Choreiform | 81 | 74.3 | 32 | 78.0 | 49 | 72.1 | .48 | 1.08 |
| Enuresis | 27 | 24.8 | 10 | 24.4 | 17 | 25.0 | .01 | .98 |
| Clumsiness | 17 | 15.6 | 10 | 24.4 | 7 | 10.3 | 3.86* | 2.37 |
| Deterioration in school performance | 20 | 18.3 | 10 | 24.4 | 10 | 14.7 | 1.60 | 1.66 |

| | Total (n=109) | | PANDAS (n=41) | | Without PANDAS (n=68) | | PANDAS vs. Without PANDAS | |
|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | Chi² | Risk Ratio |
| Motor overflow/pronator drift | 69 | 63.3 | 30 | 73.2 | 39 | 57.4 | 2.75 | 1.28 |
| Rising titers or + GAS culture + Dramatic onset | 38 | 34.9 | 26 | 63.4 | 12 | 17.6 | 21.4**** | 3.46 |
| Rising titers or +GAS culture + Definite remissions | 44 | 40.3 | 25 | 61.0 | 19 | 27.9 | 11.6*** | 2.18 |
| Sum  Rising titers or + GAS culture +Dramatic onset +Definite remissions | 26 | 23.9 | 19 | 46.3[a] | 7 | 10.3 | 18.3**** | 4.50 |

\* = $p < .05$;

\*\* = $p < .01$;

\*\*\* = $p < .001$;

\*\*\*\* = $p < .0001$

[a] = Percentages are based on available data. A number of cases were missing titer information necessary to categorize as rising/not rising; and (to a lesser degree) as high/not high.

[b] = Chi² could not be determined, as at least one expected cell frequency was less than 5. (Fisher Exact Probability Test indicated $p > .05$.

**Table 3**

Titer Assessments by Groups

| | PANDAS (N = 39)[*] | Without PANDAS (N = 60)[*] | $\chi^2$ | p |
|---|---|---|---|---|
| | *# (%)* | *# (%)* | | |
| **Elevated ASO** | 23 (59) | 22 (37) | 4.7 | .03 |
| **Elevated Anti-DNaseB** | 19 (49) | 24 (40) | .73 | .39 |
| **Elevated Anti-A$_{CHO}$** | 14 (36) | 15 (25) | 1.4 | .24 |
| **No elevations** | 0 (0) | 22 (37) | 40.1 | <.0001 |
| **One Titer Elevations** | 16 (41) | 16 (27) | 2.2 | .13 |
| **Two Titer Elevations** | 21 (54) | 19 (32) | 4.8 | .03 |
| **Three Titer Elevations** | 2 (5) | 3 (5) | § | .66 |

[*] Based on collected samples at baseline visit

§ = Chi$^2$ could not be determines, as at least on expected cell frequency was less than 5. (Fisher Exact Probability Test indicated p> .05.