Symptoms of Pediatric Feeding Disorders Among Individuals with 3q29 Deletion Syndrome: A Case-Control Study

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ABSTRACT: Objective: The goal of this study was to evaluate symptoms of pediatric feeding disorder in a sample of individuals with 3q29 deletion syndrome (3q29Del). Previous research has found that individuals with 3q29Del may experience elevated feeding concerns in early childhood; however, the specificity of these feeding concerns is not well understood. Methods: We compared individuals with 3q29Del (N = 83) with controls (N = 59) using an 11-item survey that assessed commonly reported symptoms associated with pediatric feeding disorders. An exploratory analysis also examined individuals with 3q29Del with and without a comorbid global developmental delay (GDD) or an autism spectrum disorder diagnosis. Results: Caregivers of 3q29Del cases reported higher incidences of feeding concerns on 10 of the 11 items included in the survey. This included statistically significant differences in food refusal behaviors, rejection of 1 or more food groups, and a history of failure to thrive. Parents of children with comorbid GDD were more likely to report concerns regarding food selectivity and problem behaviors during mealtime. Conclusion: The results suggest individuals with 3q29Del experience increased symptoms of pediatric feeding disorder that may require targeted evaluation and intervention for optimal outcomes. Future research should include a more thorough multidisciplinary evaluation to further elucidate symptom severity and optimal treatment strategies.

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Index terms: 3q29 deletion syndrome, feeding disorders, genomic disorder, feeding problems, 3q29 registry, ARFID.
Neurodevelopmental phenotypes account for a significant burden of disability and include intellectual disability (34%), ASD (38%), executive function deficits (46%), and graphomotor weakness (78%). Psychiatric illness manifests across the life span with psychosis prodrome (15%), psychosis (20%), anxiety disorders (40%), and attention-deficit/hyperactive disorder (63%). Neuro-imaging studies revealed structural anomalies of the posterior fossa, without accompanying motor symptoms. A recent evaluation of craniofacial dysmorphology reveals that many subjects have a prominent forehead (48.4%), prominent nose tip (35.5%), and thin upper lip vermilion (25.8%), but there is no characteristic facies that would permit clinical identification in the absence of a genetic test. Deficits in cognitive ability, though present, are generally mild to moderate and do not correlate with the overall burden of neurodevelopmental and psychiatric comorbidity.

Pediatric feeding disorder involves severe disruptions in nutritional and caloric intake exceeding ordinary variations in hunger, food preference, and/or interest in eating. Restriction in food intake may present as food selectivity (i.e., eating a narrow variety of foods and/or rejecting one or more food groups) and/or food refusal (i.e., eating a restricted volume of food resulting in formula or feeding tube dependence). Individuals who severely restrict the volume and/or variety of foods consumed during meals meet the diagnostic criteria for Avoidant and Restrictive Food Intake Disorder (ARFID). Manifestations of ARFID include paltering growth, nutritional deficiencies, and the need for oral nutrition supplementation or tube feeding to support growth and meet energy and nutrient needs. Many complex factors contribute to the development of this level of feeding concern in pediatric populations, including behavioral and environmental variables, oral motor skill deficits, and/or medical or anatomical abnormalities. Case in point, it is well-established that there is a higher incidence of feeding disorders among individuals with ASD and GDD, as well as children with predisposing medical conditions (e.g., congenital or acquired respiratory, cardiac, and gastrointestinal problems). Children with ARFID and food selectivity most often present with comorbid developmental conditions including ASD and/or GDD; children with ARFID and formula or feeding tube dependence most often present with complex medical histories. In both cases, problem behaviors during meals (tearful protests or tantrum) often maintain restricted intake of food.

Provisional evidence suggests that as many as 64% of children with 3q29Del experience elevated feeding problems during the first year of life. Available evidence, however, does not provide specific detail regarding the nature of feeding problems in this pediatric population. The purpose of this study was 2-fold. The primary aim was to evaluate symptoms of pediatric feeding disorders in a sample of individuals with 3q29Del relative to a control sample. A secondary aim was to analyze pediatric feeding symptoms among individuals with 3q29Del and comorbid GDD or ASD, relative to individuals with 3q29Del without GDD or ASD. In the process, this study provides insight into the topography and prevalence of feeding problems associated with 3q29Del.

METHODS

Recruitment

Individuals with a diagnosis of 3q29 deletion syndrome (3q29Del) were ascertained through the existing 3q29 registry housed at Emory University (3q29.org), as previously reported. In brief, recruitment of study subjects, informed consent, assent, Health Insurance Portability and Accountability Act authorization, and data collection are all enabled by the registry website. Recruitment is multifactorial and targeted to reach the stakeholder community. On launch of the registry in 2013, e-mails bearing information about the registry were sent to health care providers, medical geneticists, genetic counselors, and support organizations. The registry is also advertised through an internet campaign (Google AdWords), wherein a series of specific keywords were chosen to target the website. Registry information may also be included in the clinical genetics report that is returned to families on a positive genetic test. Individuals who register and complete informed consent have a personal profile page, in which they can complete data collection instruments. Answers may be submitted by an individual with 3q29Del or a family member (usually a parent or guardian) if the 3q29 deletion patient is underage or not capable of submitting answers. Documents can be uploaded to the registry website, and it is requested but not required that participants upload their clinical genetics report indicating a diagnosis of 3q29Del. For the current study, the inclusion criteria were as follows: clinical documentation or parent report of 3q29Del and a completed medical history and feeding questionnaire. The exclusion criterion was nonfluency in English. Study subjects of any age and with any comorbid condition were eligible to participate.

The goal of this study was to assess whether feeding problems in 3q29Del are elevated as compared with the general population; we therefore recruited a typically developing sample of control study subjects. These individuals were recruited through e-mails sent to intramural CDC and Emory University Listservs that invited a community sample to fill out surveys in an identical fashion to cases. The exclusion criterion for controls involved a clinical diagnosis of a neurodevelopmental disorder. Emory University’s Institutional Review Board (Emory University) approved this study.

Measurement

Data collection instruments exist within the registry; answers may be submitted by an individual with 3q29Del or a family member (usually a parent or guardian) if the patient is underage or not capable of submitting answers. At
enrollment, the 3q29 registry collects baseline information about the participant (i.e., the individual with 3q29Del), including sex and birthdate, and contact information for both the participant and the informant. Additional characterization occurs through a custom medical and demographic questionnaire deployed within the registry that includes 7 health-related domains that were intentionally prioritized for data collection based on medical issues previously noted in 3q29Del individuals, including self-report of autism spectrum disorder (ASD) and global developmental delays.

In 2016, we developed and deployed into the registry an 11-item questionnaire that covered common symptoms associated with pediatric feeding disorder, manifestations of Avoidant and Restrictive Food Intake Disorder, and/or signs of malnourishment based on our clinical and research experience supported by a review of the extant literature (see supplement 1: Feeding Questionnaire, Supplemental Digital Content 1, http://links.lww.com/JDBP/A325). Items included in the questionnaire covered signs of food refusal (e.g., “The participant relies on a feeding tube to meet his/her nutritional needs.” “The participant accepts little or no food by mouth.”), food selectivity (“The participant is highly selective about the foods he/she consumed during meals.” “The participant rejects most items from one of more food group (i.e., fruits, vegetables, protein, or starch).”), current or previous malnutrition (e.g., “The participant is currently failure to thrive.” “The participant has been diagnosed with anemia, now or at any time in the past.”), and feeding skill concerns (“The participant does not feed himself/herself.” “The participant only consumes smooth (e.g., yogurt) or pureed foods.”). All 11 items involve a “yes” or “no” response format. Item 7 involved a stem that allowed respondents to provide further detail about food group rejection in response to a positive response; item 9 involved a stem that provided more detail regarding specific behavior problems encountered during meals.

**Table 1.** Characteristics of Study Participants With 3q29Del and Controls

| Variable                        | Control, N = 59 (41.5%) | 3q29Del, N = 83 (58.5%) | p     |
|---------------------------------|-------------------------|-------------------------|-------|
| Age, yr, mean (range) a         | 10.5 (1.70–41.6)        | 9.4 (0.19–64.0)         | 0.456 |
| Sex, male, n (%)                | 30 (50.8%)              | 48 (57.8%)              | 0.410 |
| Comorbid diagnosis, n (%) a     |                         |                         |       |
| Autism                          | 0 (0%)                  | 20 (24.1%)              | <0.001|
| Gastrointestinal concerns       | 9 (15.3%)               | 55 (66.3%)              | <0.001|
| Global developmental delay      | 0 (0%)                  | 41 (49.4%)              | <0.001|
| Intellectual disability         | 0 (0%)                  | 18 (21.7%)              | <0.001|
| None of the above               | 50 (84.8%)              | 13 (15.7%)              |       |

*Note: We coded variables from the medical questionnaire (age at completion, sex, and autism diagnosis) as follows: age at completion, numerical value in years; sex, male yes/no; and autism diagnosis, yes/no. For the feeding questionnaire, we coded the 9 of 11 core variables as yes/no. For item 7, we coded the stem of total food group rejection as a count (range 0–4) to reflect the total number of rejected groups. For item 9, we coded the stem of food refusal behaviors as a count (range 0–8) to reflect the total problem behaviors. We first summarized continuous and discrete variables in a univariate fashion, comparing cases with controls using $t$ tests for continu- ous data and $\chi^2$ or Fisher’s exact test for discreet data. We then performed multivariate analysis, adjusting for age and sex. Specifically, analyses for total food group refusals and food refusal behaviors involved negative binomial regression, assessing each outcome as a count. We calculated rate ratios as unadjusted and adjusted for covariates (i.e., age and sex). We analyzed the remaining outcome variables involving dichotomous (yes vs no; e.g., picky eater and tube dependency) variables using binary logistic regression. We calculated odds ratios unadjusted and adjusted for covariates. When expected frequency counts were less than 5, we used exact binary logistic regression. When odds ratios could not be calculated because of zero observations in a $2 \times 2$ contingency table cell, we reported Fisher’s exact $p$ values. To assess the effect of ASD as a potential comorbidity in participants with 3q29Del, we conducted a subanalysis comparing 3q29Del study subjects with and without a self-report ASD diagnosis. We performed all analyses in SAS v.9.4 (Cary, NC) or R version 4.0.2.

**RESULTS**

**Participant Characteristics**

Table 1 provides a description of the study sample. Eighty-three 3q29 deletion syndrome (3q29Del) registrants (50.8% male) were included in this study, ranging in age from 0.19 to 64 years (mean = 9.4 years). Of the 83 responses, 81 (97.6%) were contributed by a parent or caretaker; 2 (2.4%) were completed by the 3q29 proband. Fifty-nine control participants (50.84% male) were included in the study, after excluding 1 control participant reporting a clinical diagnosis of a neurodevelopmental disorder. The sample of participants with...
3q29Del reported high rates of gastrointestinal concerns (66.3%), global developmental delays (GDDs) (49.4%), autism spectrum disorder (ASD) (24.1%), and intellectual disability (21.7%).

**Feeding Concerns in 3q29 Deletion Syndrome Versus Controls**

Participants with 3q29Del indicated more feeding concerns on 10 of the 11 items on the questionnaire when compared with the control cohort (Table 2). Six of the 83 participants with 3q29Del (7.3%) reported relying on feeding tube supplementation, and 10 (12.1%) reported relying on oral formula supplementation; neither issue was present with controls (p values 0.04 and 0.005, respectively). Thirty-five children with 3q29Del (43.8%) reported a history of failure to thrive, compared with 7.7% of controls (p < 0.001). After controlling for age and sex, statistically significant differences between the groups were found on 10 of the 11 questionnaire items. This included a significantly greater number of 3q29Del respondents indicating concerns regarding lack of consuming food by mouth (15.7% in cases vs 0% in controls, p value < 0.001).

**Table 2.** Adjusted Risks and Odds of Outcomes for Patients with 3q29Del vs. Control Patients (N = 142)

| Outcome | Control, N = 59 (41.5%) | 3q29Del, N = 83 (58.5%) | Unadjusted Ratio (95% CI) | Adjusted Ratio (95% CI) | p<sup>a</sup> |
|---------|-------------------------|-------------------------|--------------------------|------------------------|-------------|
| Signs of food refusal | | | | | |
| Tube dependency<sup>b</sup> | No 59 (100%) 76 (92.7%) Reference Reference | Reference Reference | 0.040 |
| Yes 0 (0%) 6 (7.3%) NA NA | | | |
| Formula dependency<sup>b</sup> | No 59 (100%) 73 (87.9%) Reference Reference | Reference Reference | 0.005 |
| Yes 0 (0%) 10 (12.1%) NA NA | | | |
| No food by mouth<sup>b</sup> | No 58 (100%) 70 (84.3%) Reference Reference | Reference Reference | 0.001 |
| Yes 0 (0%) 13 (15.7%) NA NA | | | |
| Signs of food selectivity | Highly selective eater | No 49 (83%) 34 (41%) Reference Reference | Reference Reference | <0.001 |
| Yes 10 (17%) 49 (59%) 7.04 (3.14, 15.9) 6.94 (3.08, 15.6) | | | |
| Food group refusal, mean ± SD | 0.2 ± 0.6 0.8 ± 1.1 3.61 (1.76, 7.38) 3.50 (1.71, 7.18) | | | 0.001 |
| Signs of behavioral concerns | Food refusal behaviors, mean ± SD | 0.1 ± 0.5 1.7 ± 2.0 17.2 (6.80, 43.4) 15.5 (6.15, 38.9) | | | <0.001 |
| Signs of malnutrition | History failure to thrive<sup>b</sup> | No 58 (100%) 45 (56.2%) Reference Reference | Reference Reference | <0.001 |
| Yes 0 (0%) 35 (43.8%) NA NA | | | |
| Currently failure to thrive<sup>b</sup> | No 59 (100%) 72 (86.7%) Reference Reference | Reference Reference | 0.003 |
| Yes 0 (0%) 11 (13.3%) NA NA | | | |
| History anemia | No 56 (96.5%) 55 (66.3%) Reference Reference | Reference Reference | <0.001 |
| Yes 2 (3.5%) 28 (33.7%) 14.3 (3.24, 62.5) 16.9 (3.72, 76.9) | | | |
| Signs of feeding skill concern | Smooth food only | No 56 (98.2%) 76 (91.6%) Reference Reference | Reference Reference | 0.266 |
| Yes 1 (1.8%) 7 (8.4%) 5.15 (0.62, 43.5) 3.44 (0.39, 30.3) | | | |
| Does not feed self | No 58 (98.3%) 64 (77.1%) Reference Reference | Reference Reference | 0.011 |
| Yes 1 (1.7%) 19 (22.9%) 17.2 (2.23, 125) 14.7 (1.88, 111.1) | | | |

N (%) unless otherwise noted. Analyses of N (%) involved odds ratio (OR); count items involved rate ratio (RR). RR is the rate ratio based on negative binomial regression and assesses the rate of outcome in 3q29 versus the rate of outcome in control. OR is the odds ratio based on logistic regression and assesses the odds of outcome in 3q29 versus the odds of outcome in control. When the expected count is <5, exact binary logistic was used. *p values based on sex-adjusted and age-adjusted generalized linear regression model ratios. aCannot estimate odds ratio because of 0 cells; presented p values based on Fisher’s exact test. NA, not applicable.

Bold indicates statistically significant results at p < 0.05.
as well as significantly higher odds of participants with 3q29Del being reported as a selective eater (odds ratio [OR] = 6.94; confidence interval [CI] = 3.08, 15.6, p value < 0.001), not self-feeding (OR = 14.7; CI = 1.88, 111.1, p value = 0.011), and having a history of anemia (OR = 16.9; CI = 3.72, 76.9, p value < 0.001), relative to control participants. The number of food refusal behaviors in participants with 3q29Del was 15.5 times higher (mean ± SD: 1.7 ± 2.0) than that of controls (mean ± SD: 0.1 ± 0.5, p value <0.001). Similarly, the number of food groups refused in participants with 3q29Del was 3.50 times higher (mean ± SD: 0.8 ± 1.1) than controls (mean ± SD: 0.2 ± 0.6, p value < 0.001). The specific topography of each behavior and food group are presented in Figures 1 and 2, respectively.

**Age-Related Feeding Problems in 3q29Del**

We also performed a descriptive analysis within the 3q29 deletion sample by age, grouped using a modified version of the age stages defined according to National Institute of Child Health and Human Development pediatric terminology, as cited in Ref. 29, shown in Supplementary Table 1 (Supplemental Digital Content 1, http://links.lww.com/JDBP/A325). These data reveal that some feeding problems are at their highest prevalence in the youngest age groups and diminish as study subjects age (tube dependency, formula dependency, no food by mouth, eats smooth foods only, or does not feed self). Other feeding problems manifest with equal frequency across the life span (highly selective eater, history of failure to thrive, currently failure to thrive, and history of anemia). In addition, the mean number of food groups refused and the mean number of food refusal behaviors are stable across age groups. These data indicate that while specific feeding symptoms may wax and wane with age, feeding problems in general are a persistent manifestation of 3q29Del.

**Feeding Concerns in 3q29 Deletion Syndrome with and Without Comorbid Global Developmental Delays**

Forty-one participants with 3q29Del (49.4%) reported a comorbid GDD diagnosis (Table 3). After controlling for age and sex, we identified a significantly higher number of food refusal behaviors for individuals with 3q29Del and comorbid GDD compared with those without GDD. The number of food refusal behaviors reported in participants with 3q29Del and comorbid GDD was 2.69 times higher (mean ± SD: 2.6 ± 2.3) than those without comorbid GDD (mean ± SD: 0.95 ± 1.4, p value <0.001). In addition, individuals with GDD were 2.54 times more likely to be described as a highly selective eater (p = 0.046) relative to those without GDD and were 3.21 times more likely to have a history of failure to thrive (p = 0.01).

**Feeding Concerns in 3q29 Deletion Syndrome with and Without Comorbid Autism Spectrum Disorder**

Twenty participants with 3q29Del (24.1%) reported a comorbid ASD diagnosis (Table 4). Age differed significantly between these groups: Individuals with a comorbid ASD diagnosis were of age 7.1 years on average (p = 0.018). After controlling for age and sex, individuals with ASD were 9.58 times more likely to report eating smooth foods only (p = 0.022). No other significant differences were found between the 2 groups.

**DISCUSSION**

Previous research has found that individuals with 3q29 deletion syndrome (3q29Del) report significant challenges with feeding in the first years of life. The purpose of this study was to conduct a preliminary analysis of the specific behavioral and nutritional concerns related to pediatric feeding disorder within this population relative to a control sample. We obtained data in a systematic fashion using a targeted instrument in the largest sample of 3q29 deletion cases available. The initial data indicate a significantly higher proportion of individuals with 3q29Del experience symptoms related to pediatric feeding disorder, with higher rates of concerns on 10 of the 11 survey items. This includes concerns regarding total refusal of 1 or more food groups and increased food refusal behaviors during mealtimes. Of note, reported risk of most variables...
was substantial; individuals with 3q29Del were 15 times more likely to report food refusal behaviors, including crying, negative statements, throwing food and utensils, spitting food, elopement, and aggression. Similarly, rates of total refusal of all foods from 1 or more food groups were 3.5 times higher in this population, with 40% of participants refusing all items from at least 1 food group. Finally, individuals with 3q29Del reported higher rates of tube and formula dependence and poorer self-feeding skills and were more likely to have a history of anemia or failure to thrive. This is the first systematic survey of feeding behaviors in study subjects with 3q29Del.

Food selectivity occurs frequently among children with global developmental delays (GDDs) and autism spectrum disorder (ASD)\(^9,14\); these are both common comorbid diagnosis within the 3q29Del population.\(^1\) Understanding how feeding concerns differ across individuals in this population with and without GDD or ASD can help practitioners better identify those at greater risk within the 3q29Del population.\(^1\) Within the 3q29Del sample, individuals with GDD were more likely to show symptoms of food selectivity and engage in food refusal behaviors during mealtimes. Interestingly, although GDD was more indicative of a number of feeding concerns, individuals with ASD only reported higher incidences of consuming soft or puree foods. Although both of these groups are at increased risk of developing a feeding disorder, GDD seems to be a stronger risk factor of feeding concerns within our 3q29Del sample.

**Implications**

This study has a number of important implications for children with 3q29Del. Participants with 3q29Del are already at increased risk of neurodevelopmental deficits. Micronutrient deficiency, insufficient caloric intake, and poor growth can have significant impacts on cognitive development and may exacerbate the neurodevelopmental concerns in this population. Children who present with feeding problems also frequently experience compromised immune functioning, may require recurrent hospitalizations, or in the most severe cases, may need placement of medically costly and invasive nasogastric or gastrostomy tubes to maintain caloric and nutritional intake.\(^21,22\) In addition, parents of children with pediatric feeding disorder report high rates of emotional distress,\(^25\) which can directly affect the socioemotional functioning of caregivers and children\(^24,25\) and cause disruption in the overall parent-child relationship.\(^26,27\)

Given the cognitive, developmental, and psychosocial implications of pediatric feeding disorder for participants with 3q29Del, it is essential that screening for feeding concerns be a part of the standard assessment protocol for this population. Effective treatments for treating feeding problems are available. In severe cases, current best practice recognizes intensive multidisciplinary intervention as a standard of care to expand oral food intake and reduce dependence formula or enteral nutrition supplementation.\(^28\) A systematic review of these practices found an average 70% success rate for a full wean from enteral feeding and a 74% increase in oral consumption of foods.\(^16\) Better screening and triage to treatment can help prevent or reduce the negative impact of poor nutrition on childhood growth and development and therefore should be a high priority for pediatricians working with children with 3q29Del.

**Limitations**

This study, although conducted on the largest known sample of individuals with 3q29Del, is not without limitations. The data were collected through self-report from parents or caregivers; self-report data can have poor reliability and validity.\(^29\) Because this was an initial survey of pediatric feeding concerns in 3q29Del, no data were collected on the intensity or frequency on reported behaviors, and the severity of the feeding symptoms remains unknown. The participants in the control group were screened out for neurodevelopmental disorders, which are associated with...
increased risk of developing a feeding disorder. When this study was launched, it was not known that GDD would amplify the risk of feeding problems in our study sample. As such, we did not include a GDD comparison group. Given our results indicating that participants with 3q29Del with GDD are at higher risk of feeding problems, this additional comparison is warranted in future research.

### Table 3. Adjusted Risks and Odds of Outcomes for Patients with 3q29Del, GDD+ Versus GDD− (N = 83)

| Characteristic                                      | Without GDD, N = 42 (50.6%) | With GDD, N = 41 (49.4%) | Unadjusted Ratio (95% CI) | Adjusted Ratio (95% CI) | \( p^a \) |
|-----------------------------------------------------|-----------------------------|--------------------------|---------------------------|--------------------------|--------|
| **Sex**                                             |                             |                          |                           |                          |        |
| Female                                              | 18 (42.9%)                  | 17 (41.5%)               | —                         | —                        | 0.898  |
| Male                                                | 24 (57.1%)                  | 24 (58.5%)               | —                         | —                        | 0.300  |
| **Age, mean ± SD**                                  | 10.5 ± 12.2                 | 8.3 ± 5.9                | —                         | —                        |        |
| **Signs of food refusal**                           |                             |                          |                           |                          |        |
| Tube dependency                                     | 39 (95.1%)                  | 37 (90.2%)               | Reference                 | Reference                | 0.633  |
| Formula dependency                                  | 2 (4.9%)                    | 4 (9.8%)                 | 2.09 (0.28, 24.4)         | 2.36 (0.28, 30.4)        |        |
| No food by mouth                                    | 38 (90.5%)                  | 35 (85.4%)               | Reference                 | Reference                | 0.426  |
| Yes                                                  | 4 (9.5%)                    | 6 (14.6%)                | 1.62 (0.35, 8.48)         | 2.46 (0.43, 17.0)        |        |
| **Signs of food selectivity**                       |                             |                          |                           |                          |        |
| Highly selective eater                              | 22 (52.4%)                  | 12 (29.3%)               | Reference                 | Reference                |        |
| Yes                                                  | 20 (47.6%)                  | 29 (70.7%)               | 2.66 (1.08, 6.57)         | 2.54 (1.02, 6.35)        | 0.046  |
| Food group refusal, mean ± SD                       | 0.5 ± 1.0                   | 1.0 ± 1.2                | 1.92 (0.97, 3.80)         | 1.92 (0.96, 3.83)        | 0.067  |
| **Signs of behavioral concerns**                    |                             |                          |                           |                          |        |
| Food refusal behaviors, mean ± SD                   | 2.6 ± 2.3                   | 2.78 (1.58, 4.93)        | 2.69 (1.56, 4.63)         |                          | 0.001  |
| **Signs of malnutrition**                           |                             |                          |                           |                          |        |
| History failure to thrive                           | 28 (70%)                    | 17 (42.5%)               | Reference                 | Reference                | 0.014  |
| Yes                                                  | 12 (30%)                    | 23 (57.5%)               | 3.16 (1.26, 7.94)         | 3.22 (1.26, 8.17)        |        |
| Currently failure to thrive                         | 39 (92.9%)                  | 33 (80.5%)               | Reference                 | Reference                | 0.119  |
| Yes                                                  | 3 (7.1%)                    | 8 (19.5%)                | 3.15 (0.77, 12.9)         | 3.09 (0.75, 12.8)        |        |
| **History anemia**                                  |                             |                          |                           |                          |        |
| No                                                   | 27 (64.3%)                  | 28 (68.3%)               | Reference                 | Reference                | 0.859  |
| Yes                                                  | 15 (35.7%)                  | 13 (31.7%)               | 0.84 (0.34, 2.08)         | 0.92 (0.35, 2.38)        |        |
| **Signs of feeding skill concern**                  |                             |                          |                           |                          |        |
| Smooth food only                                     | 40 (95.2%)                  | 36 (87.8%)               | Reference                 | Reference                | 0.148  |
| Does not feed self                                   | 2 (4.8%)                    | 5 (12.2%)                | 2.75 (0.42, 30.5)         | 6.47 (0.63, 281)         |        |
| Yes                                                  | 34 (81%)                    | 30 (73.2%)               | Reference                 | Reference                | 0.263  |
| Does not feed self                                   | 8 (19%)                     | 11 (26.8%)               | 1.56 (0.55, 4.39)         | 1.99 (0.60, 6.60)        | 0.63   |

\(^{a}\) \( p \) values based on sex-adjusted and age-adjusted generalized linear model ratios. GDD, global developmental delay; NA, not applicable.

### FUTURE DIRECTIONS

This is the first study specifically evaluating pediatric feeding concerns within the 3q29 deletion syndrome (3q29Del) population, benefiting from the largest cohort of 3q29 deletion study subjects available. Subsequent studies should conduct direct assessments of feeding...
issues to determine the severity and prevalence of feeding concerns. This should include a multidisciplinary approach aimed at identifying the behavioral, medical, nutritional, and skill-based profile of pediatric feeding disorder in this population. A larger sample size would also permit well-powered subgroup analyses. Finally, because 3q29Del is comorbid with several other neurodevelopmental and medical disorders that are associated with pediatric feeding disorder, including intellectual disability, developmental delay, and various gastrointestinal conditions, having comparison groups with these conditions would add value to any future analysis.

### Table 4. Adjusted Risks and Odds of Outcomes for Patients with 3q29Del, ASD+ Versus ASD− (N = 83)

| Characteristic, N (Row %) | Without ASD, N = 63 (75.9%) | With ASD, N = 20 (24.1%) | Unadjusted Ratio (95% CI) | Adjusted Ratio (95% CI) | p* |
|--------------------------|-------------------------------|---------------------------|--------------------------|-------------------------|----|
| Sex                      |                               |                           |                          |                         |    |
| Female                   | 29 (46%)                      | 6 (30%)                   | Reference                | Reference               | 0.206 |
| Male                     | 34 (54%)                      | 14 (70%)                  | Reference                | Reference               | 0.018 |
| Age, mean ± SD           | 7.5 ± 6.9                     | 15.6 ± 13.7               | Reference                | Reference               | 0.018 |
| Signs of food refusal    |                               |                           |                          |                         |    |
| Tube dependency          |                               |                           |                          |                         |    |
| No                       | 56 (90.3%)                    | 20 (100%)                 | Reference                | Reference               | 0.328 |
| Yes                      | 6 (9.7%)                      | 0 (0%)                    | NA                       | NA                      |     |
| Formula dependency       |                               |                           |                          |                         |    |
| No                       | 53 (84.1%)                    | 20 (100%)                 | Reference                | Reference               | 0.108 |
| Yes                      | 10 (15.9%)                    | 0 (0%)                    | NA                       | NA                      |     |
| No food by mouth         |                               |                           |                          |                         |    |
| No                       | 52 (82.5%)                    | 18 (90%)                  | Reference                | Reference               | 1.000 |
| Yes                      | 11 (17.5%)                    | 2 (10%)                   | 0.53 (0.05, 2.79)        | 1.16 (0.09, 9.06)       |    |
| Signs of food selectivity|                               |                           |                          |                         |    |
| Highly selective eater   |                               |                           |                          |                         |    |
| No                       | 26 (41.3%)                    | 8 (40%)                   | Reference                | Reference               |     |
| Yes                      | 37 (58.7%)                    | 12 (60%)                  | 1.05 (0.38, 2.94)        | 1.37 (0.44, 4.29)       | 0.593 |
| Food group refusal, mean ± SD | 0.7 ± 1.1              | 1.0 ± 1.2              | 1.37 (0.63, 2.99)        | 1.66 (0.73, 3.80)       | 0.231 |
| Signs of behavioral concerns |                           |                           |                          |                         |    |
| Food refusal behaviors, mean ± SD | 1.8 ± 1.9                  | 1.7 ± 2.5              | 0.96 (0.47, 1.99)        | 1.41 (0.65, 3.03)       | 0.376 |
| Signs of malnutrition    |                               |                           |                          |                         |    |
| History failure to thrive|                               |                           |                          |                         |    |
| No                       | 35 (57.4%)                    | 10 (52.6%)                | Reference                | Reference               | 0.559 |
| Yes                      | 26 (42.6%)                    | 9 (47.4%)                 | 1.21 (0.43, 3.41)        | 1.40 (0.46, 4.29)       |     |
| Currently failure to thrive|                             |                           |                          |                         |    |
| No                       | 55 (87.3%)                    | 17 (85%)                  | Reference                | Reference               | 0.746 |
| Yes                      | 8 (12.7%)                     | 3 (15%)                   | 1.21 (0.19, 5.81)        | 1.75 (0.23, 10.5)       |     |
| History anemia           |                               |                           |                          |                         |    |
| No                       | 43 (68.3%)                    | 12 (60%)                  | Reference                | Reference               | 0.660 |
| Yes                      | 20 (31.7%)                    | 8 (40%)                   | 1.43 (0.51, 4.06)        | 1.31 (0.40, 4.27)       |     |
| Signs of feeding skill concern |                           |                           |                          |                         |    |
| Smooth food only         |                               |                           |                          |                         |    |
| No                       | 59 (93.7%)                    | 17 (85%)                  | Reference                | Reference               | 0.022 |
| Yes                      | 4 (6.3%)                      | 3 (15%)                   | 2.57 (0.34, 16.8)        | 9.58 (1.50, NA)         |     |
| Does not feed self       |                               |                           |                          |                         |    |
| No                       | 49 (77.8%)                    | 15 (75%)                  | Reference                | Reference               | 0.115 |
| Yes                      | 14 (22.2%)                    | 5 (25%)                   | 1.16 (0.28, 4.19)        | 4.66 (0.74, 35.5)       |     |

N (%) unless otherwise noted. Analyses of N (%) involved odds ratio (OR); count items involved rate ratio (RR); RR is the rate ratio based on negative binomial regression and assesses the rate of outcome in 3q29+ ASD versus the rate of outcome in 3q29-ASD; OR is the odds ratio based on binary logistic regression and assesses the odds of outcome in 3q29 + ASD versus the odds of outcome in 3q29-ASD. When the expected count is < 5, exact binary logistic was used.*p values based on sex-adjusted and age-adjusted generalized regression model ratios. **Cannot estimate odds ratio because of 0 cells; presented p values based on Fisher's exact test. ***Upper bound could not be estimated because of few stratified observations within the adjusting covariates. ASD, autism spectrum disorder; NA, not applicable.

Bold indicates statistically significant results at p < 0.05.
CONCLUSION

This study found that participants with 3q29 deletion syndrome (3q29Del) report a number of concerns related to pediatric feeding disorder, including significant disruptive mealtime behaviors, total refusal of all foods from 1 or more food groups, picky eating, poor self-feeding skills, and a history of anemia and failure to thrive. Because this population is already at risk of developmental and physiological deficits and delays, it is essential that feeding problems be identified and addressed in early childhood. Early treatment of malnutrition or poor caloric intake holds benefit for health and overall development. For these reasons, clinicians working with patients with 3q29Del are encouraged to screen for symptoms associated with pediatric feeding disorder and, if warranted, refer for a multidisciplinary evaluation. Future research should evaluate specific nutritional, oral motor, and behavioral problems to identify the topography and severity of pediatric feeding disorder associated with 3q29Del.

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