SPECIAL ARTICLE

# Characteristics of Children Whose Siblings Have Fetal Alcohol Syndrome or Incomplete Fetal Alcohol Syndrome

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## ABSTRACT

OBJECTIVE. To describe the clinical features of American Indian children born just before and just after a sibling with fetal alcohol syndrome or incomplete fetal alcohol syndrome.

METHODS. Two retrospective case-control studies were conducted of Northern Plains American Indian children with fetal alcohol syndrome or incomplete fetal alcohol syndrome identified from 1981 to 1993 by using *International Classification of Diseases, Ninth Revision, Clinical Modification* code 760.71.

RESULTS. Compared with the controls, the 39 siblings born just before children with fetal alcohol syndrome (study 1) and 30 siblings born just before children with incomplete fetal alcohol syndrome (study 2) had more facial dysmorphology (23.1% and 16.7%, respectively), growth delay (38.5% and 10.0%), and central nervous system impairment (48.7% and 33.3%). The 20 siblings born just after children with fetal alcohol syndrome (study 1) and 22 siblings born just after children with incomplete fetal alcohol syndrome (study 2) had more facial dysmorphology (20.0% and 9.1%, respectively), growth delay (45.0% and 22.7%), and central nervous system impairment (50.0% and 31.8%) than the control siblings.

CONCLUSIONS. The "before" siblings had characteristics of fetal alcohol syndrome that could have predicted that the next child was at risk for fetal alcohol syndrome. The "after" siblings had better outcomes than the previous siblings with fetal alcohol syndrome, a finding that was associated with a decrease in maternal alcohol consumption during the after-sibling pregnancy. *Pediatrics* 2009;123:e526–e533

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**Key Words**
fetal alcohol syndrome, fetal alcohol spectrum disorders, American Indian, siblings, alcohol

**Abbreviations**
FAS—fetal alcohol syndrome
IHS—Indian Health Service
CNS— central nervous system
FASD—fetal alcohol spectrum disorders
OR— odds ratio
CI— confidence interval
SIDS—sudden infant death syndrome

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FETAL ALCOHOL SYNDROME (FAS) is the most common cause of preventable mental retardation in the United States.[1] One purpose of this study was to determine if American Indian siblings born just before a child with FAS had enough characteristics of FAS that one could predict that the next child would have FAS. This is the first epidemiologic study to describe the clinical features and hospitalization rates of siblings born just before and just after children with FAS or some characteristics of FAS (incomplete FAS) compared with control siblings and to compare siblings of children with FAS to siblings of children with incomplete FAS.

Case studies have provided general characteristics of children whose sibling has FAS.[2] The younger children typically have more complications of FAS than the older siblings when a mother continues to use alcohol with subsequent pregnancies.[2–4] Mothers who have 1 child with FAS are more likely to have additional children with more severe characteristics of FAS.[2–4]

## METHODS

The protocol was reviewed and approved by the Aberdeen Area Indian Health Service (IHS) and the national IHS institutional review boards and by 4 Northern Plains tribes. The Aberdeen Area institutional review board prohibits publication of the names of the tribes and communities participating in the study.

At 4 Northern Plains IHS hospitals or clinics, children with FAS or incomplete FAS were identified from 1981 to 1993 by using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code 760.71.[5] This code includes noxious influences (specifically alcohol) affecting the fetus or newborn through the placenta or breast milk and includes FAS.

This study uses the terms study 1, study 2, FAS, incomplete FAS, before sibling, and after sibling. These terms are defined as follows:
Study 1: Children who had all 5 of the FAS criteria.
Study 2: Children who had 1 to 4 of the FAS criteria.
FAS: FAS case subjects were defined as children who met all 5 of the following criteria: (1) prenatal alcohol exposure or maternal history of alcohol consumption; (2) FAS diagnosed or noted as a suspected diagnosis by a physician; (3) 1 or more facial features characteristic of FAS; (4) growth deficiency (any measurement of height, weight, or head circumference at ≤10th percentile for age); and (5) central nervous system (CNS) dysfunction[6] (study 1).
Incomplete FAS: If children met only 1 to 4 of the above-listed criteria, they were defined as children having incomplete FAS (study 2).
Before sibling: The child born just before a sibling with FAS or incomplete FAS.
After sibling: The child born just after a sibling with FAS or incomplete FAS.

As the children did not meet the diagnostic criteria for partial FAS, the term "incomplete FAS" is used to define the children in study 2. The Institute of Medicine definition of partial FAS requires the children to have facial features characteristic of FAS and either growth retardation or CNS neurodevelopmental abnormalities.[7,8] Facial features were not always documented in the children's medical charts; therefore, partial FAS could not be used to describe the children with incomplete FAS. Partial FAS is 1 diagnosis of the fetal alcohol spectrum disorders (FASD). FASD describe a range of structural anomalies and behavioral and neurocognitive disabilities caused by prenatal alcohol exposure. The Institute of Medicine has defined alcohol-related effects to include both alcohol-related birth defects and alcohol-related neurodevelopmental disorder.[8]

Of 142 children's medical charts in the 4 communities that had an *International Classification of Diseases, Ninth Revision* code of 760.71, 43 (30%) met 5 FAS case criteria (index cases with FAS). Of the remaining 99 medical charts, 35 that met 1 to 4 FAS case criteria were randomly selected by using a computer program to generate a list of the numbers in random order (index cases with incomplete FAS). For each case child with FAS, 2 control children were selected from the same race and same community of residence: one who was the child born immediately before the birth of the child with FAS or the child with incomplete FAS and one who was the child born immediately after the case child. If the control child had FAS, the next nearest child born by date was selected. The initial studies had 43 index case children who had FAS compared with 86 control children (study 1), and the second study had 35 index case children with incomplete FAS compared with 70 control children (study 2).

Medical charts were abstracted for the siblings born just before and just after the case children with FAS and incomplete FAS and their controls. The same variables were abstracted and analyzed for both the before and after siblings. Each case and control had potentially 6 medical charts with multiple volumes to abstract for the index child, mother, before and after siblings, maternal grandmother, and father of the index child. Because funding was insufficient to abstract all 99 incomplete FAS cases, a random sample of 35 cases for study 2 was selected. The methods used for both studies were identical and have been described.[9] The characteristics of the mothers and index children with FAS were described in separate studies.[9,10]

This report contains 4 separate analyses of data: one based on 39 siblings born just before the index case children with FAS compared with 63 control children (study 1), the second based on 30 siblings born just before the index case children with incomplete FAS compared with 46 control children (study 2), the third based on 20 siblings born just after the index case children with FAS compared with 60 control children (study 1), and the fourth based on 22 siblings born just after the index case children with incomplete FAS compared with 53 control children (study 2). In addition, the before and after siblings of the index case children with FAS were compared with the before and after siblings of the index case children with incomplete FAS.

A matched analysis was completed by using corrected McNemar's $\chi^2$ and correlated $t$ tests to determine statistical significance of differences in categorical and continuous variables.[11,12] Fisher's exact test was used for discrete variables when there were <5 expected observations in ≥1 of the cells of a 2-by-2 table. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to assess the strength of the associations. $P$ values of ≤.05 and ORs with 95% CIs that did not overlap 1.00 were considered to be statistically significant.

## RESULTS

Study 1 before and after siblings had an average of 2.0 FAS criteria, whereas study 2 before and after siblings had an average of 1.2 FAS criteria. On the basis of the case definition and compared with the control siblings, study 1 before siblings had more facial features characteristic of FAS, growth delay, CNS impairment, maternal alcohol history, and prenatal alcohol exposure and were diagnosed more often with FAS by physicians. Study 1 before siblings had significantly greater growth delay compared with study 2 before siblings (Table 1). In study 1, 5 before siblings and 2 after siblings met all 5 criteria of the case definition. In study 2, 1 before sibling and 3 after siblings met all 5 criteria of the FAS case definition. In study 1, 5 control siblings were diagnosed with FAS by a physician (Table 1).

The gender distribution for study 1 before siblings was 47.1% male and 52.9% female, and for study 2 was 40.7% male and 59.3% female ($P$ = .62). The study 1 after-sibling gender distribution was 44.4% male and 55.6% female, and the study 2 after-sibling gender distribution was 57.1% male and 42.9% female ($P$ = .43). On July 1, 1996, the mean ages of before study 1 and 2 children were 12.2 and 12.6 years, respectively, and after study 1 and 2 children were 9.1 and 7.5 years. The study 1 siblings who were deceased included:

**TABLE 1 Siblings With Characteristics of FAS by Using the Case Definition**

| | Study 1 | | | Study 2 | | |
|---|---|---|---|---|---|---|
| | Cases | Controls | OR (95% CI) or *P* | Cases | Controls | OR (95% CI) or *P* |
| Before siblings, *n* | 39 | 63 | | 30 | 46 | |
| Facial features, % | 23.1 | 0.0 | .001 | 16.7 | 0.0 | .01 |
| Growth delay, %[a] | 38.5 | 11.1 | 5.0 (1.64–15.72) | 10.0 | 2.2 | 5.0 (0.43–131.55) |
| CNS impairment, % | 48.7 | 19.0 | 4.04 (1.52–10.86) | 33.3 | 13.0 | 3.33 (1.0–12.26) |
| Maternal alcohol history, % | 82.1 | 49.2 | 3.71 (1.35–10.19) | 76.7 | 41.3 | 5.14 (1.35–28.95) |
| Alcohol use during before-sibling pregnancy, % | 64.1 | 12.7 | 11.83 (2.94–47.60) | 46.7 | 2.2 | 18.14 (2.72–789.16) |
| Diagnosed with FAS by physician, % | 16.7 | 0.0 | .001 | 10.0 | 0.0 | .06 |
| After siblings, *n* | 20 | 60 | | 22 | 53 | |
| Facial features, % | 20.0 | 1.7 | 14.7 (1.37–372.77) | 9.1 | 1.9 | 5.2 (0.34–154.11) |
| Growth delay, % | 45.0 | 13.3 | 5.32 (1.46–19.86) | 22.7 | 1.9 | 15.29 (1.53–371.71) |
| CNS impairment, % | 50.0 | 18.3 | 4.45 (1.31–15.42) | 31.8 | 11.3 | 3.66 (1.0–14.96) |
| Maternal alcohol history, % | 85.0 | 63.3 | 2.80 (0.76–18.85) | 90.9 | 47.2 | 7.80 (1.54–39.62) |
| Alcohol use during after-sibling pregnancy, % | 45.0 | 18.3 | 3.00 (0.76–13.33) | 40.9 | 11.3 | 13.50 (1.60–113.75) |
| Diagnosed with FAS by physician, % | 25.0 | 5.0 | 6.33 (1.13–38.71) | 13.6 | 0.0 | .02 |

[a] Differences between study 1 and study 2 cases are statistically significant.

- 3 before case children, 2 from sudden infant death syndrome (SIDS) and 1 fell from a building;
- 1 before control child from Meckels diverticulitis;
- 1 after case child from congestive heart failure, atrial septal defect, and cerebral edema; and
- 1 after control sibling whose cause of death was not recorded.

The study 2 siblings who were deceased included:

- 1 before control child whose cause of death was not recorded; and
- 1 after control sibling from SIDS, with abuse suspected.

### Pregnancy Outcome and Growth Delay

Compared with the control siblings, study 1 before and after siblings had significantly lower mean birth weight, length, and head circumference and postnatal growth delay in height, weight, and head circumference. Study 1 before siblings had significantly lower postnatal growth delay, height, weight, and head circumference than their controls and study 2 before siblings (Table 2). Study 1 after siblings had a significantly lower mean gestational age at birth than their controls and study 2 after siblings. Study 1 after siblings had significantly lower birth weight, smaller birth head circumference, and smaller postnatal head circumference than the study 2 after siblings. Documentation of "failure to thrive" by medical providers occurred significantly more often for study 1 after siblings than for the control siblings (Table 2).

### Dysmorphic Facial Features, CNS Impairment, and Other Problems

Dysmorphic facial features were reported more often for both the study 1 before and after siblings. Compared with the control before siblings, the only specific facial feature that had statistical significance was a low nasal bridge in the study 1 before siblings. More study 1 after siblings had "facial features" recorded in their medical charts without specific features identified than the control siblings and the study 2 after siblings (Table 3).

The most common CNS problems were behavior problems and developmental delays for both the study 1 before and after siblings. Study 1 before siblings also experienced significantly more speech/language delays, microcephaly, seizures, conduct disorder, and ptosis than their controls. More of the study 1 before siblings had ptosis than the study 2 before siblings (Table 3).

Study 1 before siblings had significantly more "other problems" than their control siblings (Table 3). These other problems included numerous gray hairs at 14 years, impulsive behavior, difficulty with supination, poor memory, myopia, wide intercanthal distance, visual difficulties, abnormal dermatoglyphics, malocclusion of upper right incisor, fearlessness, easily angered, dolichocephaly, hemangioma, poor sleep pattern, crying spells, hirsutism, and nystagmoid movements of the eye.

### Hospitalizations

Study 1 before siblings were hospitalized a significantly greater number of days and had more otitis media than their controls. Study 2 before siblings had significantly more hospitalizations and a greater number of days hospitalized than their controls. None of the differences in hospitalization data for the study 1 and study 2 after siblings were statistically significant (Table 4).

### Social Services Involvement

In addition to health complications, study 1 and study 2 before and after siblings were removed from their homes more frequently than their controls. Study 1 before siblings were removed from their homes and placed in foster care more frequently than the controls and study 2 before siblings. Study 1 after siblings were removed from their homes and placed in foster care more frequently than their controls. Study 2 after siblings were removed from their homes more fre-

**TABLE 2 Pregnancy Outcomes and Growth Delay for Before and After Siblings**

| | Study 1 | | | Study 2 | | |
|---|---|---|---|---|---|---|
| | Cases | Controls | OR (95% CI) or *P* | Cases | Controls | OR (95% CI) or *P* |
| Before-sibling neonatal outcome, *n* | 39 | 63 | | 30 | 46 | |
| Mean gestational age, wk | 39.0 | 39.4 | .40 | 39.4 | 38.7 | .40 |
| Mean birth weight, g | 2987 | 3477 | .003 | 3190 | 3353 | .35 |
| Mean birth length, cm | 49.3 | 51.8 | .004 | 50.5 | 52.5 | .10 |
| Mean head circumference, cm | 33.4 | 34.6 | .01 | 34.5 | 35.5 | .15 |
| Before-sibling postnatal growth delay | | | | | | |
| Growth delay (≤10th percentile), %[a] | 46.9 | 12.7 | 6.00 (1.61–22.31) | 12.5 | 2.6 | 5.29 (0.43–143.50) |
| Height (≤10th percentile), %[a] | 35.7 | 7.5 | 4.38 (1.34–14.28) | 8.3 | 2.6 | 3.36 (0.22–101.70) |
| Weight (≤10th percentile), %[a] | 45.2 | 7.3 | 6.29 (1.74–22.66) | 8.3 | 2.6 | 3.18 (0.20–96.33) |
| Head circumference (≤10$^{th}$ percentile), %[a] | 44.0 | 4.3 | 17.68 (3.04–134.22) | 11.1 | 3.2 | 3.75 (0.23–115.87) |
| After-sibling neonatal outcome, *n* | 20 | 60 | | 22 | 53 | |
| Mean gestational age, wk[a] | 37.8 | 39.2 | .02 | 40.2 | 40.0 | .50 |
| After-sibling low birth weight (<2500 g) | | | | | | |
| Mean birth weight, g[a] | 2945 | 3438 | .002 | 3498 | 3470 | .89 |
| Mean birth length, cm | 49.6 | 51.7 | .02 | 51.3 | 52.2 | .41 |
| Mean head circumference, cm[a] | 33.5 | 35.1 | .005 | 35.6 | 35.2 | .54 |
| After-sibling postnatal growth delay | | | | | | |
| Failure to thrive, % | 22.2 | 0.0 | .04 | 9.5 | 0.0 | .48 |
| Growth delay (≤10th percentile), % | 52.9 | 14.0% | 6.89 (1.75–28.26) | 26.3 | 2.3 | 9.00 (0.90–94.08) |
| Height (≤10th percentile), % | 37.5 | 12.7% | 9.5 (1.05–85.57) | 21.1 | 0.0 | .06 |
| Weight (≤10th percentile), % | 43.8 | 7.3% | 9.92 (1.99–53.38) | 21.1 | 2.3 | 7.00 (0.60–315.11) |
| Head circumference (≤10th percentile), %[a] | 57.1 | 4.2% | 30.67 (4.27–284.6) | 22.2 | 0.0 | .09 |

[a] Differences between study 1 and study 2 cases are statistically significant.

**TABLE 3 Facial Features, CNS Impairment, and Cardiac and Skeletal Problems of Before and After Siblings**

| | Study 1 | | | Study 2 | | |
|---|---|---|---|---|---|---|
| | Cases | Controls | OR (95% CI) or *P* | Cases | Controls | OR (95% CI) or *P* |
| Before-sibling dysmorphic facial features, *n* | 39 | 63 | | 30 | 46 | |
| Any facial features, % | 23.1 | 0.0 | .001 | 16.7 | 0.0 | .13 |
| Philtrum, % | 10.3 | 0.0 | .06 | 13.3 | 0.0 | .25 |
| Low nasal bridge, % | 12.8 | 0.0 | .02 | 10.0 | 0.0 | .25 |
| Palpebral fissures, % | 12.8 | 0.0 | .09 | 6.7 | 0.0 | .32 |
| Thin upper lip, % | 12.8 | 0.0 | .09 | 6.7 | 0.0 | .32 |
| Before-sibling CNS impairment | | | | | | |
| Behavior problems, % | 41.0 | 14.3 | 10.50 (2.16–50.93) | 33.3 | 8.7 | 3.57 (0.91–14.08) |
| Developmental delay, % | 17.9 | 4.8 | 5.25 (1.03–26.76) | 10.0 | 4.3 | 1.20 (0.16–9.26) |
| Speech/language delay, % | 25.6 | 11.1 | 3.63 (1.05–12.53) | 16.7 | 2.2 | 6.00 (0.62–57.68) |
| Microcephaly, % | 10.3 | 0.0 | .04 | 3.3 | 0.0 | .82 |
| Seizures, % | 20.5 | 7.9 | 5.40 (1.09–26.84) | 3.3 | 4.3 | 2.0 (0.13–31.98) |
| Conduct/behavior disorder, % | 12.8 | 1.6 | 9.00 (1.03–78.58) | 3.3 | 4.3 | 0.60 (0.05–7.46) |
| Ptosis, %[a] | 30.8 | 15.9 | 3.27 (1.02–12.26) | 3.3 | 0.0 | .83 |
| Other problems, % | 17.9 | 7.9 | 5.50 (1.07–28.36) | 16.7 | 2.2 | 9.00 (0.91–219.16) |
| After-sibling dysmorphic facial features, *n* | 20 | 60 | | 22 | 53 | |
| Any facial features, % | 20.0 | 1.7 | 14.75 (1.35–379.22) | 9.1 | 1.9 | 4.00 (0.36–44.11) |
| Facial features present but not specified, %[a] | 20.0 | 1.7 | 14.75 (1.35–379.22) | 0.0 | 0.0 | 0.0 |
| After-sibling CNS impairment | | | | | | |
| Behavior problems, % | 45.9 | 8.3 | 14.00 (1.67–117.28) | 31.8 | 5.7 | 5.0 (1.02–24.46) |
| Developmental delay, % | 25.0 | 1.7 | 19.67 (1.92–488.91) | 31.8 | 1.9 | 24.27 (2.56–578.00) |

[a] Differences between study 1 and study 2 cases are statistically significant.

quently and had more unknown placements than the controls (Table 5).

## DISCUSSION

This is one of the first studies to describe the characteristics of siblings born just before and just after a child with FAS or incomplete FAS. A small number of the siblings were deceased at the time of the study. Siblings of children with FAS have been found to have an increased mortality rate.[3,4,13,14] Three siblings (2 cases and 1 control) died of SIDS. SIDS has been associated with prenatal alcohol exposure and binge drinking in the first trimester in Northern Plains American Indians.[15] Although FAS has been identified in males more fre-

**TABLE 4** Before- and After-Sibling Hospitalizations

| | Study 1 | | | Study 2 | | |
|---|---|---|---|---|---|---|
| | Cases | Controls | OR (95% CI) or *P* | Cases | Controls | OR (95% CI) or *P* |
| Before siblings, *n* | 39 | 63 | | 30 | 46 | |
| Ever hospitalized, % | 64.1 | 57.1 | 0.70 (0.26–1.81) | 56.7 | 45.7 | 0.69 (0.22–2.06) |
| Total No. of hospitalizations | 67 | 72 | .12 | 46 | 36 | .03 |
| Total days hospitalized | 547 | 277 | .002 | 244 | 103 | .03 |
| Average No. of hospitalizations | 1.72 | 1.14 | .12 | 1.53 | .78 | .03 |
| Average days hospitalized | 14.03 | 4.40 | .002 | 8.13 | 2.24 | .03 |
| Hospital diagnosis of otitis media, % | 30.8 | 15.9 | 3.27 (1.02–12.26) | 23.3 | 10.9 | 2.77 (0.58–17.51) |
| After siblings, *n* | 20 | 60 | | 22 | 53 | |
| Ever hospitalized, % | 45.0 | 45.0 | 1.00 (0.26–3.65) | 40.9 | 58.5 | 0.52 (0.15–1.84) |
| Total No. of hospitalizations | 26 | 81 | .74 | 25 | 48 | .57 |
| Total days hospitalized | 114 | 307 | .85 | 151 | 144 | .23 |
| Average No. of hospitalizations | 1.30 | 1.35 | .74 | 1.14 | .91 | .57 |
| Average days hospitalized | 5.70 | 5.12 | .85 | 6.86 | 2.72 | .23 |

None of the differences between study 1 and study 2 cases are statistically significant.

**TABLE 5** Before and After Siblings in Social Service Placement

| | Study 1 | | | Study 2 | | |
|---|---|---|---|---|---|---|
| | Cases | Controls | OR (95% CI) or *P* | Cases | Controls | OR (95% CI) or *P* |
| Before siblings, *n* | 39 | 63 | | 30 | 46 | |
| Removed from their home, %[a] | 77.1 | 20.0 | 12.04 (2.86–107.63) | 48.1 | 18.6 | 7.00 (1.43–34.33) |
| In foster care, %[a] | 51.3 | 9.5 | 12.14 (2.84–109.32) | 23.3 | 6.5 | 7.50 (.83–68.09) |
| After siblings, *n* | 20 | 60 | | 22 | 53 | |
| Removed from their home, % | 72.2 | 15.5 | 14.16 (3.47–62.14) | 61.9 | 14.3 | 6.29 (1.69–35.08) |
| In foster care, % | 60.0 | 10.0 | 18.5 (2.24–152.64) | 27.3 | 7.5 | 3.67 (0.73–21.77) |
| In unknown placement, % | 0.0 | 0.0 | 0.0 | 27.3 | 0.0 | .004 |

[a] Differences between study 1 and study 2 cases are statistically significant.

quently than in females,[16–18] the gender differences in this study were not significant.

Children diagnosed with FAS will have growth delay, facial features characteristic of FAS, and CNS impairment.[7,8] Siblings of the index case children had more prenatal growth delay (lower birth weights and heights and smaller head circumferences) than their controls. Postnatal growth delay was documented in height, weight, and head circumference for the siblings of the index case children and has been reported previously.[3,19] The study 1 before-sibling growth delay was significantly greater compared with the controls and study 2 before siblings. This difference in growth delay between the 2 studies could be associated with a greater percentage of the study 1 mothers using alcohol during the before pregnancy. Of the before mothers, 64.1% of the study 1 mothers and 46.7% study 2 mothers used alcohol during the before-sibling pregnancy. With the after-sibling cases, 45.0% of the study 1 mothers and 40.9% of the study 2 mothers used alcohol during this pregnancy compared with 100% of the study 1 mothers and 60.0% of the study 2 mothers who used alcohol during the previous pregnancy of the children with FAS and incomplete FAS.[20] Although fewer study 1 mothers used alcohol during the after pregnancy, the after siblings had significantly shorter gestation, lower birth weight, and smaller head circumference than the controls and study 2 case children. Perhaps these smaller birth outcomes are caused by decreased liver function that occurs in women with chronic alcohol use.[21] The study 1 and study 2 mothers delivered children with FAS or incomplete FAS at mean ages of 26.6 and 28.0 years, respectively, which is younger than ages reported in previous studies.[2,22–25] Perhaps these mothers began drinking alcohol at an earlier age, which contributed to the smaller outcomes of the after siblings.[10] The after siblings also had more failure to thrive compared with the control siblings. Failure to thrive has been found in children with FAS.[2,26,27]

The facial features recorded in the case-sibling medical charts were characteristic of FAS.[7,8,19,28] A low nasal bridge found in the before siblings may be more commonly identified because this feature is easier to visualize. Short palpebral fissures generally require a measurement to identify this feature.[19] Because specific facial features were not always recorded for both the before and after siblings, physicians may need additional training to recognize the facial features of FAS. Physicians can be trained in ~2 days to diagnosis FAS accurately.[29] Facial features characteristic of FAS are required for a diagnosis of FAS, partial FAS, and alcohol-related birth defects.[7,8] Physicians need to record the specific facial features of FAS in the children's medical charts.

The before siblings had numerous CNS impairments compared with their controls. The most common impairments included behavior problems,[3,7–9,14,27,30–32] developmental delays,[3,7–9,27,30,32] speech and language delays,[3,7–9,14,27,31,32] microcephaly,[3,9,27] seizures,[2,3,5,9,27] and

ptosis,[9,19] which have also been found in other FAS studies. The association of seizures with prenatal alcohol exposure has been known since the late 1800s.[2] Study 1 had 20% of the before siblings experiencing seizures, which was similar to seizure rates reported in other studies of children with FAS (range: 3.3%–30.2%).[2,9,27] The siblings born just before the children with FAS had characteristics of FAS including facial features, growth deficiencies, and CNS impairments indicated the next child was at risk for having FAS if the mother continued to use alcohol and there were no intervention efforts with the mother. Clinicians need to refer these mothers for chemical-dependency assessments.

On the basis of the literature, the study 1 after siblings should have had more complications than their siblings with FAS.[2–4] The after siblings had 1.2 of the FAS case definition criteria and had 2 significant CNS impairments including more behavior problems and developmental delays, which are consistent with FAS.[3,7–9,14,27,30–32] The improved outcome of the after siblings was associated with a reduction in alcohol use during the pregnancy from 100% in the case pregnancy to 45% with the after pregnancy,[20] which is not consistent with other studies.[2–4] However, behavior problems and learning delays have caused difficulty for the children and their families in their homes, schools, and communities.[33]

The control mothers also had used alcohol during pregnancy. In study 1, 12.7%, 19.8%, and 18.3% of the control mothers drank alcohol with the before-sibling, index-sibling, and after-sibling pregnancies, respectively. Of these study 1 control mothers, 6.7% drank heavy amounts of alcohol during the after-sibling pregnancy.[20] Thus, it is not surprising that 5% of the after control siblings were diagnosed with FAS by a physician. These 3 children had 2 to 4 criteria of the case definition.

Case studies of specific families have found siblings of children with FAS to have characteristics of FAS.[2–4,14] These studies have found that the siblings experience more impairment with each child born to a mother who drinks heavy amounts of alcohol during pregnancy.[3,4] A popular belief is that women who have a child with FAS do not decrease alcohol consumption during pregnancy.[34] However, this study found that the siblings born after the children with FAS or incomplete FAS had fewer characteristics of FAS than the siblings with FAS or incomplete FAS. This finding suggests that women who have drunk heavy amounts of alcohol can decrease their alcohol consumption during pregnancy. The reasons the mothers decreased their alcohol use with the after-sibling pregnancy is not known. Health care providers need to screen pregnant women for alcohol use and intervene with women who are drinking alcohol during pregnancy for more positive outcomes.

To our knowledge, hospitalization data have not been published for siblings of children with FAS or incomplete FAS. Compared with their controls, otitis media was noted more often in study 1 before siblings who were hospitalized. The rates of other conditions did not differ significantly in the siblings and their controls who were hospitalized. Consistent with other FAS studies, otitis media was more common among the children with FAS.[9,26,35] The reason study 2 before siblings had significantly more hospitalizations and a greater number of days hospitalized compared with their controls is unknown. The differences in the hospitalization rates of studies 1 and 2 after siblings and their controls were not statistically significant, which could be a result of the fairly high rates of hospitalizations for both cases and controls. Hospitalizations provide opportunities for health care providers to evaluate the children for characteristics of FAS.

Decreased alcohol use during pregnancy may have led to a reduction in hospitalization costs related to prenatal alcohol exposure in the after siblings. Children with FAS and incomplete FAS required more hospitalizations and were hospitalized more days,[9] which increases their medical care costs. Hospitalizations were likely underreported in this study, because some children could have been placed with families outside the service area of the hospital.

In addition to health care, the case siblings had needs that often required social services intervention. Other studies have reported that a high proportion of children with FAS had been removed from their homes.[4,9,16] When children are living in a home where alcohol is abused, the children are at greater risk for experiencing neglect[3] and for being removed from the home.[36] Foster care is the most common placement for children with FAS.[9,36] Social workers need to establish long-term living environments for children with characteristics of FAS to strengthen their potential to succeed.[27]

Because the mothers were not interviewed and the children were not examined, the study was limited to information available in the medical charts. Another limitation of the study is that the fathers of the before and after siblings were not identified. The siblings may have had a father who was not the father of the sibling with FAS. The genetic difference may have affected the outcome of subsequent pregnancies.

## CONCLUSIONS

Siblings of children with FAS and incomplete FAS have health, learning, and social needs. The before siblings had FAS characteristics that could have predicted that the subsequent child was at risk for FAS if the mothers continued using alcohol during pregnancy. The after siblings had 2 statistically significant CNS impairments and no significant hospitalizations that were associated with a decrease in alcohol consumption among the mothers during this pregnancy. With fewer mothers reporting alcohol use during pregnancy, the after siblings had better outcomes than their previous siblings with FAS or incomplete FAS. Additional research is needed to identify the reasons mothers abstain from alcohol during pregnancy. Health care providers need to screen and intervene with all pregnant women who drink alcohol during pregnancy. Health care providers need training to identify the characteristics of FASD. Support services for pregnant women are needed to prevent alcohol use

during pregnancy for the health and well-being of the mothers and their children.


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