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Fetal alcohol syndrome: maternal and neonatal characteristics

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1 Introduction

In 1973 Kenneth Jones and David Smith first used the term fetal alcohol syndrome (FAS) to describe a characteristic pattern of birth defects and developmental disabilities in infants born to severely alcoholic mothers [17]. Fetal Alcohol Syndrome is characterized by the following: a) growth retardation, b) neurodevelopmental abnormalities, c) characteristic facial anomalies. Although FAS has not been reported to occur without prenatal alcohol exposure, a confirmed history of maternal alcohol abuse during pregnancy is not required for diagnosis [15]. There is no safe amount of alcohol drinking during pregnancy. Figure 1 shows the cumulative effect of constant drinking throughout pregnancy. The importance of FAS as a public health problem is striking when the cost of care and the prevalence rates for the disorder are combined.

Alcohol now is the most common identifiable cause of mental retardation, surpassing Down syndrome and spina bifida [2]. Recent data indicates an incidence rate of 2.8 to 4.6 per 1000 live births for FAS. The combined rate of FAS and alcohol-related neurodevelopment defect (ARND) is close to 1% [23]. In North Dakota the incidence of FAS is about 2/1000 live births, thus 10-18 children with FAS are born in North Dakota each year [10]. Among chronic alcoholic mothers the incidence is as high as 4.3% [3]. Considering the lifetime cost of services for a patient with FAS, which is estimated to be $1.4 million, the economic impact of this preventable disorder is significant [8]. An additional area of public health concern is the recurrence risk for FAS in subsequent births, which may be as high as 25% [4]. The familial recurrence rate for FAS, when compared to the general population, is increased 85 times in older siblings of FAS children and 350 times in the younger siblings [4].

Although all pregnancies should be screened for alcohol use, not all women who drink alcohol during pregnancy give birth to FAS children. Even though alcohol is necessary, it does not appear to be a sufficient factor alone in causing alcohol-related birth defects. This means that there are other susceptibility factors involved in predisposing the fetus to alcohol effects. Identifying these risk fac-

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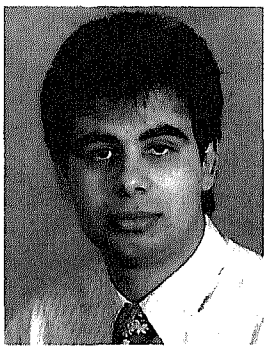

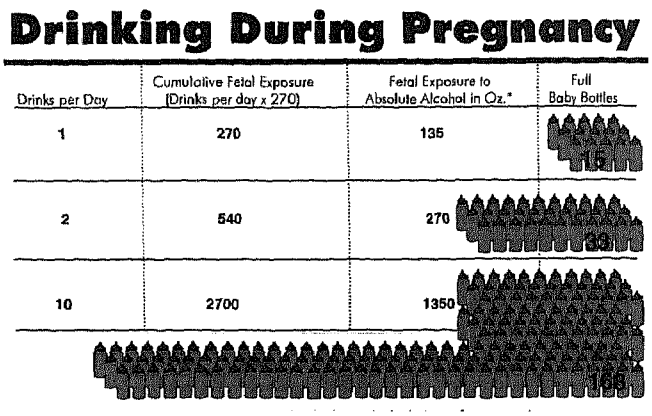

Figure 1.

tors would enable us to identify the high risk pregnant women and focus prevention efforts on these individuals. One way of identifying the risk factors is by clinical epidemiological studies comparing the FAS population to controls.

In this study we wanted to: 1) Determine the characteristics of FAS mothers. This would help family practitioners and obstetricians identify pregnant women at high risk of having a child with alcohol birth defect. 2) Find the neonatal differences between children with FAS and controls, which might be helpful in early identification of these children. 3) Briefly review the literature on risk factors of FAS.

Previous studies on risk factors for FAS have been done in the past [5, 6], but most studies have not described mothers of these children. Our approach is unique in that we sought to answer these questions by comparing birth certificate data of children who were on the North Dakota FAS registry with birth certificate data from a control population of North Dakota children. The FAS registry in North Dakota is one part of a longitudinal surveillance system for children and adults with developmental disabilities in North Dakota. The linking of the FAS registry and birth certificate data allows for complete datasets for the FAS cases and provides access to an appropriate control group with equally complete data availability.

2 Methods

Failure to diagnose FAS by physicians is partially due to the difficulty inherent in making the diagnosis [7, 15, 17]. Unfortunately there is no pathognomonic sign for FAS. Diagnosis of this syndrome is more frequent at 5-10 years of age when the diagnostic features are more distinctive. In North Dakota the diagnosis of FAS is either made or confirmed in nearly all cases by a single physician (J.T.M.). In cooperation with the state's comprehensive evaluation center, he provides genetics and dysmorphology clinics at eight locations around the state. All children on the registry with a diagnosis of FAS have been seen by J.T.M. Native American children who are suspected to have FAS are commonly referred to one of the genetics and dysmorphology clinics which are held on the reservations at the Indian Health Service clinics (IHS). The registry lists all known cases in North Dakota that have been identified by the outreach clinics, referrals from the IHS clinics, children seen at the State's Comprehensive Evaluation and Treatment program and who have been reported to the FAS center. We believe this would comprise more than 90% of identified cases of FAS in North Dakota.

In this study the standard case definition was used for the diagnosis of FAS [26]. In the more recent FAS diagnostic criteria the cases in this would correspond to categories 1 and 2 [15]. Additionally a weighted diagnostic checklist, which has been developed over several years, was used to aid in providing consistency of diagnosis and in documentation of individual signs [11].

We identified patients with a diagnosis of FAS and requested the Department of Vital Records at the North Dakota Health Department to conduct a computerized search using the child's name, birth data, and gender to identify their birth certificates. Then we searched the death certificate files for any children on the registry who may have died . Controls were children who were born within one month of the FAS child and of same sex and county of birth. The statistical methodology used is described in [10]. A matched analysis was used since the cases and controls were matched.

3 Results

Of the total FAS registry list of 228 cases, birth certificates were identified for 132 (56%) of the children. The mean age at the time of diagnosis was 7.1 years. Of the 132 cases, 106 (80.3%) were Native Americans and 24 (18.2%) were Caucasians. In this population 51 (38.6%) of the cases were male and 81 (61.4%) were female. The remaining 96 cases were either born in other states or had a name change, and their records were not identifiable. However, we did search the adoption records.

Table I presents the results of the comparisons between the FAS group and controls for the prenatal characteristics. The mothers of the FAS children began prenatal care later than the mothers of controls. Only the variables that were significant at the .05 level and above are included. 41% of FAS mothers began their prenatal care after the first trimester compared to only 20% of controls (OR: 3.05, 95% CI= 2.01-4.63, p <0.001). The mothers of the FAS children were older than the control group mothers. They also had less weight gain during pregnancy, less education, fewer prenatal visits and shorter pregnancy length. About 60% of the FAS mothers were single at the time of delivery compared to only 13% of the control mothers (OR: 10.26, 95% CI= 6.55-16.10, p<0.001). The fathers of the FAS children were about 3 years older with less education than the control group fathers.

Table I. Prenatal variables comparing children with FAS with controls. Five controls were selected for each case. Fisher exact used for p-value

Variable	N	Mean	SD	p-value
Mother's age (years)				
Case	132	27.4	5.3	<0.001
Control	660	25.4	4.7	
Father's age (years)				
Case	43	32.0	9.3	<0.001
Control	215	27.8	4.9	
Weight gain in pregnancy (lb)				
Case	33	22.1	11.4	<0.001
Control	165	30.4	11.9	
Gestation (weeks)				
Case	101	38.7	4.5	<0.001
Control	505	40.0	3.0	
Month prenatal care began				
Case	123	3.4	2.2	<0.001
Control	615	2.7	1.3	
Number prenatal visits				
Case	123	5.5	4.1	<0.001
Control	615	9.7	3.3	
Mother's education				
Case	125	10.6	1.5	<0.001
Control	625	13.0	2.0	
Father's education				
Case	32	10.8	2.2	<0.001
Control 160	13.2	2.1		

Table II. Comparison of newborn data of children with FAS with controls. Five controls were selected for each case. Fisher exact used for p-value

Variable	N	Mean	SD	p-value
Birth Weight (grams)				
Case	132	2784	636.9	<0.01
Control	660	3485	553.4	
Apgar (1 Minute)				
Case	106	7.1	1.7	<0.05
Control	530	7.5	1.5	
Apgar (5 Minute)				
Case	106	8.5	1.5	<0.01
Control	530	8.8	0.9	

Table II presents the results of comparison for the neonatal characteristics of the two groups. The FAS neonates had lower birth weights and Apgar scores. FAS infants were more likely to have congenital malformations compared to controls (OR: 4.55, 95% CI= 2.96-6.99, p<0.001).

4 Discussion

Although Native Americans make up less than 10% of North Dakota population, they comprised to 80% of the FAS cases (North Dakota Census Bureau, 1990 Census). Other studies have also reported higher prevalence of FAS in non-Caucasian, lower socioeconomic populations than populations of predominant Caucasians and middle class [3, 5, 25]. The question is whether this race predominance is due to a genetic susceptibility or related to differences in cultural and behavioral factors. In a survey conducted by the CDC's National Center for Health Statistics it was shown that 20.7% of mothers reported drinking alcohol throughout their pregnancy and of these 0.6% were frequent prenatal drinkers (six or more drinks a day) [14]. Interestingly, although prenatal drinking was higher among the upper class Caucasian women, frequent prenatal drinking was more prevalent among older non-Caucasian women of lower SES [14]. Other studies indicating heavier drinking among some ethnic minorities compared to Caucasians have also been reported [22]. This difference in the drinking behavior might indeed be one reason for the increased incidence of alcohol-related birth defects in the latter group. The drinking pattern in African-Americans, Native Americans and Caucasian women is also different. The former two groups tend to binge drink, whereas Caucasian alcoholics tend to drink constantly throughout the week [12, 18]. It has been shown that peak blood alcohol level, rather than total daily consumption is the critical factor affecting neurodevelopment in children [13, 26]. Therefore because the blood alcohol level peaks higher in binge drinkers, this could put infants of African-Americans and Native-Americans at a higher risk for FAS.

Although FAS occurs in all races, it is frequently identified in the lower SES population, regardless of race [5]. Poverty is associated with malnutrition, less education, physical abuse, smoking, drug abuse, obstetric complications, and poor prenatal and postnatal care, all which can interact and exacerbate the effects of alcohol on the fetus.

The importance of SES as a risk factor does not mean that genes have no role in FAS. In a study conducted by Streissguth et al., it was shown that the concordance rate for FAS among MZ twins was 100% but for DZ twins it was about 63% [27]. This suggests that there is a partial genetic basis for individual vulnerability to alcohol's teratogenicity. It has also been shown that there are genetic differences in alcohol metabolism between different races [24, 28]. Such differences in metabolism rate may play an important role in fetal susceptibility to alcohol.

One of the differences between the mothers of our cases and controls was older age in the former group. Other studies have demonstrated that the risk of FAS and ARBD increases with increased maternal age and parity despite similar drinking patterns [16, 25]. While the FAS mothers are about 2.5 years older than controls, a statistically significant difference (p<0.01), this difference is of limited clinical or public health value in developing strategies to identify women at high risk to have a

child with FAS. This increased vulnerability could be due to increased ratio of maternal body fat to water in older age which leads to higher peak blood alcohol levels. This in turn increases the alcohol exposure to the fetus and the risk of FAS. On the other hand, older women with a history of chronic drinking have a faster metabolism of alcohol which leads to higher acetaldehyde levels, the highly toxic metabolite of alcohol.

Another maternal characteristic identified in our study was the relatively smaller maternal weight gain during pregnancy compared to controls. This has also been reported in other studies [20, 25]. Undernutrition is commonly seen in alcoholics. In this condition the fetus will not receive the essential nutrients and vitamins necessary for normal growth and development. On the other hand even if the mothers nutrition status is normal, alcohol-induced placental dysfunction impairs the transport of amino acids, glucose and folate [21].

One of the most consistent features of FAS children is low birth weight. Alcohol-induced growth retardation has been shown in many animal experiments. The amount of growth retardation depends on the dose of alcohol consumed and the trimester of exposure. Being exposed during the latter part of pregnancy has a greater impact on birth weight than during early pregnancy [13]. FAS children also have a higher rate of congenital malformations due to the teratogenic effects of alcohol. Lower birth weight, higher incidences of congenital malformations and prematurity and the damaging effects of alcohol on the CNS, may contribute to the lower Apgar scores of FAS children in our study.

Interestingly, 42% of mothers of children with FAS began prenatal care in the second or third trimester of pregnancy compared with 20% of control mothers, suggesting that more than half of these women are seen in the first trimester of pregnancy when important opportunities to refer and support their entry into chemical dependency treatment are available. These women need to be assessed early on, since having large differences in the number of prenatal visits makes them less accessible.

It was also shown that both parents of children with FAS have less education than the controls. This parameter becomes extremely important knowing that alcohol-related birth defects are 100% preventable with abstinence. Educating the society in general and women in childbearing age specifically about the permanent deleterious effects of alcohol on the fetus is the most important way in eliminating this disorder. Primary prevention can be achieved by public education via all types of media. This effort should start early in life with the help of different institutions such as schools, health promotion organizations, and family. Primary care physicians, Obstetricians and nurse practitioners should continuously educate their patients during routine annual visits, prenatal visits, and family planning visits about alcoholism and pregnancy. Fathers should also be included in the educational programs, because of their significant influence on the partner's drinking habit. The positive male role of supporting the spouse for a healthy pregnancy outcome should be emphasized. Women who have had a child with FAS or are chronic heavy-drinkers with low incomes should be reffered for appropriate counseling and birth control information and should have intensive long-term follow-ups. Not only is patient education necessary, but also primary care providers need continuing education regarding the epidemiology and importance of FAS. In a study conducted in Minnesota, one of the barriers toward screening pregnant women for alcohol use was lack of adequate training of physicians during medical school and residency in this area [19]. This could be compensated by workshops, CMEs, seminars and newsletters.

5 Limitations of this study

Although the evaluation of birth certificate data was not one of the study goals, a brief comment on the quality of the birth certificate data used in this study seems warranted. The new birth certificates were adopted by the North Dakota Division of Vital Records in 1989. In North Dakota six of eight mothers of children with FAS were incorrectly classified as having not used alcohol during pregnancy on the child's birth certificate. The mothers of only two out of eight children with FAS were correctly classified as having used alcohol on their birth certificates. This data suggests that the accuracy of this information on birth certificates may limit the usefulness of this specific variable. For this reason we were not able to compare the amount and pattern of drinking between our cases and controls. Other than this variable we believe that most of the information we used from the birth certificates are reliable. Our data extends the findings of Buescher et al.

from their study examining the accuracy of birth certificate data on alcohol use from the state of North Carolina [9].

We do not have a "gold standard" to determine the accuracy of diagnosis of patients in the registry. Some patients have been seen for second opinions at other referral centers and we have observed high rates of agreement about the diagnosis of FAS. However, the most appropriate measure would be to have a second physician see a sample of registry patients and to then compute the agreement. This has not yet been done in our State.

The data from the North Dakota registry does not allow us to control for either the effects of income, education or the different health care delivery systems (Indian Health Service) used by many Native Americans in North Dakota.

6 Conclusion

In FAS the influences and outcomes are not exclusively due to alcohol exposure [1,5]. Interactions of a variety of maternal and paternal factors at different stages of development influence the outcome of a child. The interacting and transacting effects of these variables, along with a multitude of other variables, produce a major influence upon the eventual outcome of the child. Important in this model is the understanding that many of the environmental influences after birth are potentially modifiable and can positively impact outcome.

The clinical and public health implications of this study are important. About 60% of mothers who will have a child with FAS in North Dakota could be provided with advice about drinking during pregnancy and could be offered treatment for this problem in the first trimester of pregnancy. While it would be ideal to be able to identify these women prior to pregnancy, the results of this study reinforce the need to continue to emphasize early identification and entry into treatment of drinking pregnant women. The importance of this strategy will be useful in reducing both the prevalence and severity of the alcohol related birth defects and developmental disabilities in the children of these women.

Abstract

Alcohol is the most common identifiable teratogenic cause of mental retardation in North America. Fetal Alcohol Syndrome (FAS) is a major public health problem, which is frequently under diagnosed by physicians.
Objective: To identify and quantify the maternal risk factors and neonatal characteristics of children with FAS.
Design: a retrospective case-control study using birth certificate data of North Dakota children diagnosed with FAS. Five controls were selected for each patient. Controls were selected from the computerized birth registry and matched by gender, year and month of birth.
Subjects and setting: A list of all the children diagnosed with FAS from the North Dakota FAS Registry was sent to the State Health Department. We were able to locate the birth certificates for 132 (56%) of the 228 cases on the registry.
Results: Of the 132 FAS cases, 106 (80.3%) were Native Americans and 24 (18.2%) were Caucasians. In this sample 51(38.6%) of the cases were male and 81 (61.4%) were female. Statistically significant maternal characteristics at $p<0.01$ were: older mother's age, lower education level, fewer months of prenatal care, fewer prenatal visits, lower gestational age at time of delivery and less prenatal weight gain. Significant neonatal differences at $p<0.01$ were lower birth weight and Apgar scores and higher incidence of congenital malformations.
Conclusion: FAS is a completely preventable developmental disability. Consumption of alcohol during pregnancy can result in lifelong physical and mental impairments on the fetus. All pregnant women should be screened for alcohol use during prenatal visits. Women with positive screens or at high risk should be identified early by the primary care physician and referred for treatment and counseling.

Keywords: Birth certificate, case control, fetal alcohol syndrome (FAS), prenatal characteristics, prevention, risk factors.

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