Fetal Alcohol Spectrum Disorder in Israel: Increased Prevalence in an At-Risk Population

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ABSTRACT: **Background:** Maternal exposure to alcohol during pregnancy can lead to a wide range of clinical manifestations in their offspring, termed fetal alcohol spectrum disorder (FASD). In Israel, relatively few cases of FASD have been diagnosed and the prevalence has not been systematically evaluated.

Objectives: To determine the number of children with FASD or at risk for FASD in a select population of high risk patients seen at a clinic evaluating foster and adopted children.

Methods: Israeli children under 2 years old who were candidates for domestic adoption or in foster care were prospectively evaluated for clinical manifestations of FASD, and information was obtained regarding parental use of alcohol or other illicit drugs.

Results: Of the 100 patients prospectively evaluated, 8 had mothers with a known history of alcohol consumption during pregnancy. Two of the children had fetal alcohol syndrome (FAS) without known maternal exposure to alcohol and two had partial FAS. Eleven other children were at risk for development of one of the diagnostic categories of FASD.

Conclusions: In a population of pre-adoption and foster children, 15% either had manifestations of FASD or were at risk for developing FASD. Although this is a select high risk population, the data from this study strongly suggest a greater prevalence of FASD than previously assumed. Under-diagnosis of FASD is detrimental to affected children who could benefit from interventions designed to meet the needs of FASD victims.

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KEY WORDS: adoption, alcohol, birth defects, fetal alcohol syndrome (FAS), fetal alcohol spectrum disorder (FASD)

Fetal alcohol spectrum disorder is the leading cause of acquired developmental delay in the world [1]. FASD is caused by ethanol consumption throughout pregnancy, especially during the first trimester. Since ethanol is a teratogen, fetal cellular exposure to this toxin causes birth defects associated with dysmorphic features (e.g., smooth philtrum, thin upper lip, small palpebral fissures, upturned nose, microcephaly), other birth anomalies, neurodevelopmental abnormalities, and neuroanatomic defects [1,2]. The effects of in utero exposure of the fetus to alcohol are long term and are associated with developmental disabilities, cognitive impairments, psychiatric disorders, and social maladjustment [2,3]. The diagnosis of FASD is important for the patient and family since early intervention, appropriate medical follow-up, and social support are crucial for improving outcome and quality of life of both the patients and their families [4].

FASD is highly prevalent in many countries for which statistics are available. It is estimated that the prevalence of FASD among younger schoolchildren may be as high as 2%–5% in the United States and some West European countries [5]. In an Italian study the rate of FASD reached 4.1% in children attending 25 primary schools in the Lazio region [6]. Based on epidemiologic studies, risk factors for having a child with FASD have been identified; these include mothers in their teenage years, single mothers, previous children with FASD, and adopted children from Eastern Europe [7].

The number of children with the diagnosis of FASD in Israel is extremely low and there are no registries or databases in Israel listing children suspected of having FASD. Senecky et al. [8] reported that during a 10 year period (1998–2007), only six patients with a diagnosis of FASD were listed in two of the four health insurance funds in Israel. This may reflect a true low incidence, a lack of awareness among health professionals regarding the diagnostic features of FASD, the absence of systematic data collection in Israel related to FASD, confusion regarding the updated diagnostic criteria of FASD as related to classical fetal alcohol syndrome, or unawareness of the importance of listing FASD as a diagnostic entity [8]. With regard to the possibility of FASD being rare in Israel, this would be quite unlikely given the increase in alcohol consumption in the country [9], a lifestyle among a large segment of the population that is similar to western countries where the prevalence of FASD is high [10,11], and lack of awareness on the part of expectant mothers and adolescent girls regarding the minimal amounts of alcohol that are considered toxic [12,13].

We investigated a group of children at high risk for FASD. The Medical Unit for Adoption and Foster Care at Hadassah

***Dr. Tenenbaum and Dr. Wexler contributed equally to the study**

FASD = fetal alcohol spectrum disorder

Medical Center evaluates Israeli infants and children referred by the Child Services Unit of the Ministry of Welfare and Social Services who are in foster care, are residing in institutions, are candidates for adoption or were recently adopted. We evaluated this group to determine the level of fetal exposure to alcohol and the frequency of children having clinical manifestations consistent with FASD.

PATIENTS AND METHODS

The first 100 children under the age of 2 years who were referred to the medical adoption unit of Hadassah Mount Scopus for comprehensive medical and developmental assessment were prospectively evaluated regarding epidemiological and clinical manifestations of FASD. Information collected during the evaluation was recorded in the patient's medical record and subsequently collated. The study was approved by the Hadassah University Medical Center Institutional Review Board.

All children were examined by a physician, a psychologist and a nurse. The infants' medical and developmental condition and their anthropometric measurements were recorded. The medical history of the child and the biological parents was obtained. However, for many of the patients, complete information was not available either because the child had been abandoned or the parent(s) were not forthcoming with the information. As part of the evaluation, children underwent testing for human immunodeficiency virus, hepatitis, syphilis and, when indicated, other congenital infections. For children with microcephaly or cranial malformations, we recommend a neurologic evaluation and a cranial ultrasound. In nearly all cases follow-up in a child developmental center is recommended.

The diagnostic criteria for FASD and clinical manifestations associated with FASD were based on the U.S. Institute of Medicine's diagnostic classification with modifications based on a Canadian Task Force [14,15]. In brief, the diagnostic categories included:

- Fetal alcohol syndrome with known maternal alcohol exposure and with the child displaying typical dysmorphology associated with FAS (i.e., flat upper lip, flattened philtrum, midline facial hypoplasia), evidence of growth retardation, and central nervous system neurodevelopmental or neuroanatomic abnormalities
- FAS without confirmed maternal alcohol consumption with all the criteria mentioned above
- Partial FAS with confirmed maternal alcohol consumption
- Alcohol-related birth defects
- Alcohol-related neurodevelopmental disorders showing evidence of both neurodevelopmental and social/behavioral abnormalities.

FAS = fetal alcohol syndrome

RESULTS

Demographic data for children and patients are shown in Table 1. For 8% of the mothers there was a known history of alcohol consumption. Most likely this is an underestimation since information regarding alcohol exposure during pregnancy was not available for many of the mothers. This is even more true for the fathers as their identity was often unknown. As seen in Table 1, many mothers are involved in high risk behaviors such as drug use and promiscuity (e.g., prostitution, multiple partners). The median age for the children in our study population was 4.5 months and the mean age 5.9 ± 5.2 months at the initial visit. Almost all the children were evaluated prior to their first birthday.

The clinical characteristics of the children are listed in Table 2. Of the children with documented exposure to alco-

Table 1. Demographic characteristics of patients and biological parents

Patient's age (mos)	
Mean (SD)	5.9 ± 5.2
Median	4.5
Range	.5–24
Gender	
Males	42
Females	58
Religion of parents	
Jewish	59
Moslem	16
Christian	9
Mixed	13
Unknown	3
Maternal history	
Alcohol use	5
Drug use	14
Both	3
Promiscuity	3
Paternal history	
Alcohol use	0
Drug use	6
Both	2

Table 2. Clinical characteristics of patients

	Confirmed maternal alcohol consumption (n=8)	Alcohol consumption denied or unknown (n=92)
Facial dysmorphology	1	6
FAS facial characteristics	1	3
Prematurity	2	10
Low birth weight	1	11
Failure to thrive	2	13
Microcephaly	1	3
Developmental delay	0	15
Other neurological findings*	0	5

*Irritability, abnormal tone, appetite dysregulation, hearing loss, craniofacial abnormalities

hol, only two had manifestations that could be associated with partial FAS (a diagnostic category of FASD), and none had the facial dysmorphology associated with in utero alcohol exposure. One child was premature and had a low birth weight adjusted for gestational age, while the second child had microcephaly and failure to thrive.

For children with no documented in utero exposure to alcohol, one child had all the manifestations of FAS including a flat upper lip, microcephaly, low birth weight and failure to thrive. A second child, who was examined at age 12 months, also had all the features of FAS including microcephaly, failure to thrive, developmental delay, and midline facial hypoplasia. As shown in Table 2, many children without alcohol exposure had clinical characteristics associated with FASD including characteristic facial features, low birth weight or failure to thrive, and neurological deficits including developmental delay and microcephaly. Nineteen children had more than one problem. Over two-thirds of the mothers (10/14) with known drug usage but without alcohol exposure had children with one or more of the following: dysmorphism, low birth weight, failure to thrive, developmental delay, microcephaly, and/or other neurological abnormalities. This is in contrast to maternal alcohol consumption with or without drug usage where most of the children were asymptomatic.

Table 3 is a summary of our findings regarding the diagnosis of FASD. As part of our analysis, we characterized children at risk for attaining a diagnosis of FASD and this included the six children with known maternal ethanol exposure but no clinical manifestations (at risk for ARND), and five children with two of the three criteria for FAS but without confirmed maternal ethanol exposure. Of the latter five, one patient was a 5 month old child with FAS dysmorphology and developmental delay without growth failure, and the other four were children with developmental delay/microcephaly and growth failure, but without recognizable facial features of FAS.

ARND = alcohol-related neurodevelopmental disorders

Table 3. Summary of findings

FAS /+ history of alcohol exposure	0
FAS /- history of alcohol exposure	2
Partial FAS	2
ARBD	0
ARND	0
Potential to develop FASD*	5
Alcohol exposure/no signs of FASD	6

* No history of ethanol exposure but two of three clinical characteristics (FAS dysmorphology, growth failure, neurologic abnormalities)

ARBD = alcohol-related birth defects, ARND = alcohol-related neurodevelopment disorders

DISCUSSION

Among the children evaluated in a national medical adoption unit, 4% of the children met the criteria for a diagnosis of FASD, and another 11% were highly likely to receive a diagnosis of FASD either because of known alcohol exposure so that any neurologic, psychological or social adjustment abnormality discovered subsequently would place them in the category of ARND, or because they had two of three characteristics of FAS and would then meet the definition for FAS without confirmed maternal alcohol exposure.

It is likely that we are underestimating the true incidence of FASD and the number of children at risk in our population. Having a history of maternal alcohol exposure significantly impacts on the diagnosis of FASD. Without a confirmed history of maternal alcohol exposure, it is impossible to diagnose partial FAS, ARBD, or ARND so that the only diagnostic entity obtainable is FAS, which requires typical facial dysmorphology, growth failure and neurological manifestations. In contrast, in the presence of a history of maternal alcohol consumption, a child can be classified as FASD even with one of these abnormalities (partial FAS) or can be classified as ARBD or ARND if he or she has birth defects related to ethanol or neurological or social dysfunction.

In our patient population we often did not have information pertaining to the mother. Even when there was information, we could not be sure of its veracity as the information was often obtained by Child Protective Services personnel, and the parent may not have disclosed that she had consumed alcohol so as not to prejudice the legal and social status of her infant. In fact, one of the children in our study is listed as at risk for FAS without a history of maternal alcohol consumption (no information was available). Subsequently, when we examined a younger sibling, it became clear that the mother was an alcoholic who drank during her pregnancies. Based on the new information, this child should be reclassified as having FAS, thereby increasing the proportion of children with FASD to 5%.

Another reason for the underestimation of FASD in our population is that most of the children seen in our clinic were under the age of 1 year. Since many children were subsequently adopted, they were not followed in our clinic. This placed limits on our ability to diagnose FASD as many of the syndromatic and cognitive features of FASD do not become apparent until after 1 year of life. Reviewing studies performed in other countries, most children with FASD were diagnosed later in life, often after years of follow-up [5-7].

The high rate of both FASD and the risk for developing FASD in our selected population is not surprising when compared with studies conducted in other countries. FASD features were found in more than half the Russian orphans residing in

ARBD = alcohol-related birth defects

baby homes in Murmansk, Russia [16]. Similar findings were found for adopted children from Eastern Europe who were followed for a long time. Previous studies have also shown that children with FASD are over-represented in foster care and adoption [17]. For example, in a study done in Washington State, 50% of the surveyed children with FASD or FAS had at least one adoptive parent and 15.4% had foster parents [18].

A limitation of the current study is its generalizability to the general Israeli population. Clearly, the patients in our group were high risk and the incidence of FASD would be expected to be much lower among the general population of newborns. However, it would be reasonable to assume that there are mothers who ingested alcohol and did not give their children up for adoption or have them removed from the home. There are also mothers who would be considered normative and may have consumed alcohol early in the pregnancy prior to becoming aware of their pregnancy. This is quite common in other countries, and in the USA at least 50% of pregnant women drank alcohol during the 3 months prior to pregnancy recognition, and 1 in 20 of these women drank at moderate to heavy rates [19].

Our study is also in line with other recent reports suggesting an increase in alcohol abuse among Israelis, especially teenagers and young adults. This is reflected in statistics regarding the increasing abuse of alcohol in the general population [9], alcohol levels in fatal casualties in motor vehicle accidents [20], and the number of children brought to the emergency room with alcohol poisoning [21].

This raises the question why the reported incidence of FASD is so low in Israel given the findings in our study. Taking a conservative estimate that the incidence or risk of FASD in the general population is 100 to 1000 times lower than the 15% seen in our study, it would be expected that between 22.5 and 225 children born per year would be at risk for FASD (annual birth rate in Israel is approximately 150,000). This is far higher than the number of children carrying a diagnosis of FASD listed in hospitals or health insurance funds [8]. It is also far below the rates reported for other countries (USA, South Africa, Italy, Sweden) where the incidence of FASD in the general population ranges from 5% to 7% [5].

One possibility is that the rate of FASD in Israel is extremely low except in very high risk populations such as those seen in our clinic. This could be due to low rates of alcohol consumption and low rates of alcohol abuse among the different constituents of the Israeli population. While it is true that there are higher rates of abstinence in the population as compared to European countries, a large-scale survey sponsored by the Ministry of Health showed that the lifetime prevalence rate of alcohol abuse or dependence is 4.3% and that 5% of the population drank alcoholic beverages three or more times a week, which is comparable to European countries [10]. Specific segments of the population are at greater risk, including young adults, males, and immigrants from the former Soviet Union. Other studies have also shown that ethanol abuse is a significant problem among immigrants from the former Soviet Union and Ethiopia [22,23], and that the frequency of intoxication and binge drinking was increasing [9]. Hence, a low prevalence of alcohol intake or dependence is not a reason for the lower reported rates.

It is also possible that despite the high prevalence of drinking in the general population, pregnant women are very careful to avoid drinking during pregnancy. Weiss and colleagues [24] found that among 2477 woman who had given birth at a single medical center during the years 1999–2000, only 1.13% admitted to consuming alcohol during pregnancy – mostly small amounts and infrequently. However, the authors were very skeptical of their findings as they did not concur with reported prevalence rates in other countries; they suggested that there was significant under-reporting because of the fear of stigmatization, denial, and/or the reluctance to share personal information. This was borne out by a more recent survey done in 2010 sponsored by the Israel Anti-Drug Authority, which found that among 3815 postpartum women in three Israeli hospitals 17.1% reported that they consumed alcohol during pregnancy and 0.8% admitted to binge drinking at least once during the last 3 months of their pregnancy [13].

A third possibility is that there are protective genes for FASD that are either associated with diminished alcohol consumption or reduced teratogenic effects of alcohol on the fetus. The alcohol dehydrogenase 1B genotype is related to the risk for alcoholism, and there is a greater prevalence (20%) of the protective allele among Jews. While it is true that younger individuals (< 33 years old) carrying the protective allele had lower alcohol consumption (mean number of drinks per occasion 2.6), in those without the protective allele the mean number of drinks was 6.2, which is considered risky and unsafe drinking and within the ranges known to be associated with FASD [25]. There are also genes that are protective of the fetus, but there is no increased prevalence of this gene among Jews.

The most likely reason for under-reporting is the lack of awareness of health care providers or their lack of effort to either solicit a history of maternal alcohol consumption or examine children for features of FASD. In their study [8], Senecky and co-authors interviewed geneticists and child development specialists throughout Israel. Fifty percent of the respondents felt that "tens" or even "hundreds" of children with a potential diagnosis of FASD had been missed. Among the respondents, approximately 60% reported that there was low or insufficient awareness of FASD among physicians in Israel.

The current study suggests that the number of children with FASD being diagnosed is only the tip of the iceberg. This is unfortunate as early intervention may minimize many of the cognitive, behavioral and social problems associated with FASD [4]. Identification of mothers with a history of ethanol

consumption and the appropriate follow-up by the social services may prevent future cases in the same family. Attributing antisocial behavior to FASD may facilitate more appropriate interventions and lower the rate of recidivism [3].

CONCLUSIONS

This study shows that there is a high rate of FASD and a risk for developing FASD in a selected population of adopted or foster children in Israel. The study is limited in that it observed the patients for a short time and at a very early stage of development. While direct extrapolation to the general population is not possible, this study can confirm previous studies in Israel suggesting that FASD is under-diagnosed. Since intervention is important and potentially beneficial, it is crucial to identify children with FASD or at risk for developing FASD. Steps to improve the diagnosis of FASD in Israel would include large-scale studies of the pediatric population to determine the true incidence of maternal alcohol consumption and FASD as well as interventions to enhance the awareness of health care personnel regarding the need to assess pregnant women for ethanol exposure and clinical manifestations of FASD among children and adults.

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"Neither a man nor a crowd nor a nation can be trusted to act humanely or to think sanely under the influence of a great fear"

Bertrand Russell (1872-1970), British philosopher, mathematician, author, and Nobel Prize laureate

"The memories of a man in his old age are the deeds of a man in his prime"

Pink Floyd, English rock band that achieved worldwide success with their progressive and psychedelic rock music. Their work is marked by the use of philosophical lyrics, sonic experimentation, innovative album art, and elaborate live shows