Fetal Alcohol Spectrum Disorder in Israel

Yehuda Senecky MD, Dov Inbar MD, Gary Diamond MD, Lina Basel-Vanagaite MD PhD, Shmuel Rigler MD
and Gabriel Chodick PhD

1Child Development and Rehabilitation Institute, Schneider Children’s Medical Center of Israel, and 2Department of Medical Genetics, Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel
3Clalit Health Services, Netanya, Israel
4Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

ABSTRACT: Background: Fetal alcohol spectrum disorder is a range of disabilities caused by gestational exposure to alcohol. FASD is the leading cause of preventable mental retardation and developmental disability in the United States, with an incidence of 1–10 per 1000 live births. FASD in Israel has yet to be examined systematically.

Objectives: To evaluate professionals' experience, awareness and knowledge of FASD in Israel and their awareness of maternal consumption of alcohol, and to collect epidemiological data on the syndrome in Israel.

Methods: A short questionnaire was sent to all 43 program directors of genetic institutes (n=14) and child developmental centers in Israel (n=29). Four questions related to their experience and knowledge of FASD. The epidemiological survey included data from all 17 hospitals in Israel and from the two main health management organizations within the public health care system.

Results: The response rate was 98% (n=42). A total of 38.1% of respondents reported having diagnosed at least one case of FASD and fewer than 10% of respondents stated that the knowledge regarding FASD among physicians in Israel was adequate. Developmental pediatricians were more likely to have diagnosed at least one case as compared to geneticists. During the period 1998–2007 the diagnosis of FASD appeared in the records of only 4 patients from the total number of 17 hospitals in Israel. During the same period only six patients were diagnosed at the HMO within the public health care system.

Conclusions: Despite the accumulated knowledge on FASD in many countries and the increase in alcohol consumption in Israel, professionals' awareness of its potential damage is limited. Educational programs to increase physician awareness should accompany publicity campaigns warning the public of the dangers associated with alcohol consumption during pregnancy.

KEY WORDS: fetal alcohol spectrum disorder, alcohol, prenatal alcohol consumption, pregnancy

Fetal alcohol spectrum disorder constitutes a range of disabilities caused by gestational exposure to alcohol, from full-blown fetal alcohol syndrome to its partial presentation as fetal-alcohol effects [1]. When full-blown, FASD is defined by the characteristic pattern of facial abnormalities, growth retardation, brain damage, and evidence of maternal drinking during pregnancy [2]. Prenatal exposure to alcohol leads to developmental, emotional, social and behavioral problems. The characteristic facial appearance includes short palpebral fissures, short nose, smooth or flat philtrum, thin upper lip, and flattened medial midface. Associated physical abnormalities include micrognathia, abnormal position and formation of the ears, hypertelorism, epicanthic folds and palmar crease abnormalities. Congenital anomalies can include cardiac, skeletal, renal, ocular, auditory and other malformations and dysplasias.

Ethanol derivatives are associated with embryotoxicity, teratogenesis, chromosomal anomalies and mitochondrial damage [3]. Alcohol exposure contributes to damage to the structure, neuronal migration and synaptogenesis of the developing central nervous system [4]. The extent of impairment to a developing fetus depends not only on the amount of alcohol ingested, but also on the timing of drinking, the mother’s health and genetic susceptibility to alcohol and her individual rate of ethanol metabolism. Repeated binge exposure creates a high fetal risk, especially at the beginning of the pregnancy.

Alcohol exposure damages many organs and systems in the developing fetus, and the drinking habit should be taken into consideration in the differential diagnosis of developmental, learning and behavioral problems in children [5]. Fetal alcohol spectrum disorder is the leading cause of preventable mental retardation and developmental disability in the United States [6].

Knowledge of the dangers of alcohol during pregnancy is not new. In the 1720s, during the “gin epidemic” in Britain, the Royal College of Physicians reported to Parliament that parental drinking was a cause of “weak, feeble and distempered children” [7]. In fact, even the Bible notes damage to children from maternal alcohol consumption during pregnancy [8]. In the modern era, the first description of the danger of alcohol to the fetus was reported in 1957 by Rouquette [9], who followed 100 children whose parents were known alcoholics and found...
severe effects of alcohol in the children of alcoholic mothers. Similar results were reported in a later study in 1973 by Jones and co-authors [10]. Epidemiological reports in recent years from the U.S., Canada, Australia, South Africa, England and Eastern Europe on the drinking habits of women of childbearing age [11-14] found that many women consume alcohol before they become pregnant as well as during their pregnancy. The situation is complicated by the fact that many of the pregnancies are unplanned [15]. According to different reports 9.1 children out of a 1000 live births are eventually diagnosed as affected by varying degrees of severity of the syndrome [16].

In Israel, despite the reported rise in alcohol consumption and changes in drinking habits over the past two decades, there is little mention of the problem in the professional literature [17]. Over the past decade a rise in the number of adoptions to Israel from Eastern Europe and the former Soviet Union, where alcohol consumption by young women has been rampant, has done little to raise awareness of the problem among professionals. The dysmorphology and the cognitive and behavioral problems of these children in Israel are brought mainly to the child developmental experts and to the geneticists. In this article we report data on the knowledge, awareness and experience of these professionals to FASD in Israel.

**SUBJECTS AND METHODS**

All 43 child development centers and genetic counseling clinics in the country were included in the survey. A short telephone and e-mail questionnaire sought to ascertain the extent of clinical experience with FASD, estimates of its prevalence, and the need for greater awareness among clinicians involved in counseling and the delivery of antenatal care.

Data were collected between May and August 2008 by a single trained research assistant. Of the 43 centers 42 agreed to participate (response rate 98%). The study population included 29 pediatricians who head child development clinics, and 14 geneticists who serve as directors of all genetic counseling centers in Israel. The number of FASD cases from large medical centers and two large health management organizations were determined by a computerized database search using the International Classification of Diseases, Clinical Modification (ICD-9-CM) codes for FASD. A comparison of attitudes and awareness of FASD between heads of child development clinics and heads of genetic counseling centers was undertaken using a standard chi-square test.

**RESULTS**

Overall, 38.1% (16/43) of the respondents reported having diagnosed at least one case of FASD, with a significant ($P = 0.03$) difference between geneticists (14.3%) and pediatricians (50.0%). None of the study participants reported having diagnosed 10 or more cases of FASD during his/her clinical experience. Substantial differences between the study groups were noted in the perceived awareness of the dangers of antenatal alcohol exposure among colleagues in the same field of expertise. Twenty-five percent (7/28) of the child development pediatricians and one genetics program director thought that the awareness to FASD among physicians in Israel was sufficiently high. Four of the 28 pediatricians (14.1%) and none of the 14 geneticists rated the knowledge about FASD among physicians in Israel as “high” or “sufficient.” Overall, 59.5% of the study participants reported low and insufficient awareness of FASD [Table 1]. Most of

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CD = child development
the respondents estimated that there were "tens" (40.5%) or "hundreds" (9.5%) of undiagnosed FASD cases.

During the period 1998-2007 the diagnosis of FASD was recorded in only 4 patients from the total number of 17 medical centers in Israel. During the same period only six patients were diagnosed in the two HMOs within the public health care system.

**DISCUSSION**

Many children with FASD are not diagnosed because of the lack of knowledge, awareness and training among professionals in the health care system [18]. Not only is early diagnosis and treatment crucial for a better developmental outcome, but identifying a child impaired by intrauterine exposure to alcohol can prevent additional cases of FASD in the family if good antenatal counseling and care services are available [19]. The economic impact of FASD is significant; the annual cost per affected child is more than US$ 14,000 [20].

Our study is one of the first in Israel dealing with the complex issue of FASD. Information was collected from data sources of the Ministry of Health and the two main health care providers (HMOs) in the public health care system. All child developmental centers and genetic counseling clinics in the country were surveyed with regard to their experience with and knowledge of FASD. Compliance with the survey reached 98% of centers reviewed, via phone and mail questionnaire. Although 38.1% of respondents reported having diagnosed at least one case of FASD, only 10% of respondents expressed the opinion that Israeli physicians’ knowledge on FASD was adequate. This may represent an overestimation by the participants regarding their abilities and experience in diagnosing FASD. In the past. Therefore, our finding that only 10 FASD cases were identified during 1998–2007 could reflect the true incidence, although under-reporting is possible.

A survey conducted by the National Drug and Alcohol Control Authority of Israel in 2005 examined drinking habits among adults in Israel. The participants were asked about their drinking in the last year, the last month and the last week. The study discovered a significant increase in alcohol drinking: 22% declared being drunk in the last year and 18% had done binge drinking in the last month [21].

According to various reports, binge drinking during pregnancy is the most harmful to the fetus [22]. In Israel, little information is available about women who become pregnant unintentionally. According to reports from Australia, 47% of pregnancies are not planned and 58.7% reported drinking alcohol at least in the first trimester [23]. Previous surveys note that even in cases where a woman is aware of the potential damage accrued to the fetus from alcohol, she might drink unintentionally if she is unaware of the pregnancy.

The present study reflects a worrisome confluence of two potentially mutually reinforcing trends relating to efforts at preventing alcohol-related birth defects: the first is the lack of public awareness of all the ramifications of unregulated alcohol consumption by women during their childbearing years, and the second is inadequate professional knowledge and counseling services.

**CONCLUSIONS**

The results of the survey suggest the importance of improved public awareness and dissemination of information by means of continuing medical educational programs on the potential dangers to fetal development as a result of alcohol consumption by young women. This is essential to reverse a trend bound to worsen over time, judging from the experience of other countries with similar social and cultural patterns as Israel. Especially needed are controlled studies on the true extent of the problem among teenagers and young adults considered to be at highest risk for bearing children with FASD.

The relatively large proportion of conservative populations in Israel (e.g., Moslem Arabs and ultra-Orthodox Jews), with the resultant effect on patterns of alcohol consumption, namely social stigma associated with or even constraints on alcoholic consumption, might positively affect a downward trend in FASD when compared to other societies. Nevertheless, Israel has undergone significant social changes over the last few decades that resulted in increasingly westernized alcohol consumption patterns, partly due to large immigration waves from the former USSR.

As we expected prior to the study, we found low awareness and lack of knowledge, but we were astonished to discover that even those at the forefront of diagnosing, treating and preventing developmental and dysmorphic syndrome issues declared how limited their experience was in dealing with the issue in a practical way. The study results indicate that there is a gap between the increasing alcohol consumption in Israel and the limited public and professional knowledge on FASD.

**Correspondence:**

Dr. Y. Seneky
Child Development and Rehabilitation Institute, Schneider Children’s Medical Center of Israel, Petah Tikva 49202, Israel
Phone: (972-3) 925-3614
Fax: (972-3) 925-3871
email: Senekymi@zahav.net.il

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**Capsule**

**Labeling cancer cells with virus-carrying GFP**

One important aspect of medicine is the need for surgeons to distinguish between tissue to be removed and tissue to leave behind. Kishimoto et al. have demonstrated the use of a viral vector that targets tumor cells specifically, not to kill them directly, but to demarcate cancerous tissue clearly. They started with a designed adenovirus, OBP-401, which can replicate only in cells that contain an active telomerase, as in malignant tissue. This virus also contains a gene for green fluorescent protein (GFP). In a proof-of-principle study, peritoneal tumors were induced in nude mice by injecting human cancer cells containing red fluorescent protein. Twelve days later, disseminated nodules had formed, and intraperitoneal injection of the virus and examination 5 days later revealed co-localization of red and green fluorescent signals. In a similar mouse model for pleural dissemination using unlabeled human lung cancer cells, nodules that would not have been detected by eye were clearly visualized via GFP. Although other tumor-imaging approaches are available, cancer-specific labeling could add value to the idea of virus-aided, fluorescence-guided surgery. Proc Natl Acad Sci USA 2009; 106: 14514

**Capsule**

**Comprehensive mapping of long-range interactions reveals folding principles of the human genome**

The conformation of the genome in the nucleus and contacts between both proximal and distal loci influence gene expression. In order to map genomic contacts, Lieberman-Aiden et al. developed a technique to allow the detection of all interactions between genomic loci in the eukaryotic nucleus followed by deep sequencing. This technology was used to map the organization of the human genome and to examine the spatial proximity of chromosomal loci at one megabase resolution. The map suggests that the genome is partitioned into two spatial compartments that are related to local chromatin state and whose remodeling correlates with changes in the chromatin state. At the megabase scale, the chromatin conformation is consistent with a fractal globule, a knot-free, polymer conformation that enables maximally dense packing while preserving the ability to easily fold and unfold any genomic locus. The fractal globule is distinct from the more commonly used globular equilibrium model. The results demonstrate the power of Hi-C to map the dynamic conformations of whole genomes. Science 2009; 326: 289