Fetal Alcohol Spectrum Disorders among Children in a Brazilian Orphanage

Kerstin Strömland*[1], Liana O. Ventura[2], Layla Mirzaei[3], Keyla Fontes de Oliveira[4], José Marcelino Bandim[5], Adriana Parente Ivo[6], and Carlos Brandt[7]

Background: The objective was to investigate the frequency of fetal alcohol spectrum disorders (FASD) and ophthalmologic anomalies in orphanage children in Brazil. **Methods:** A prospective study was performed on 94 children living in an orphanage in Brazil. The children were examined by a multidisciplinary team consisting of specialists in pediatrics, neurology, psychology, neuropsychiatry, and ophthalmology. **Results:** The main reasons for living in the orphanage, in 61% of the children, were negligence, child abuse, and abandonment. Of all the children studied, 50% had mothers with known alcohol abuse and 47% had one or more diagnoses of neurodevelopmental/ behavioral and/or cognitive deficits. General developmental delay was found in 18%, intellectual disability in 3%, cognitive impairment in 27%, attention-deficit/hyperactivity disorder in 14%, and autism in 3%. Altogether 17% had FASD, comprising three children with fetal alcohol syndrome (FAS), six with partial FAS, and seven with alcohol-related neurodevelopmental disorder. 16% had ophthalmological findings such as poor vision, strabismus, and dysmorphology of the optic nerves. Twenty-eight children (30%) were adopted from the orphanage; of these, six had FASD (two FAS, three partial FAS, one alcohol-related neurodevelopmental disorder), five had attention-deficit/ hyperactivity disorder, and eight had developmental delay. **Conclusion:** Nearly half of the children living in the orphanage had neurodevelopmental disorders and a considerable number showed signs of damage from prenatal alcohol exposure. A broader look at the problem of FASD in Brazil and other South American countries is desirable to document the burden of disease and provide data for targeting prevention efforts.

Birth Defects Research (Part A) 103:178–185, 2015

Key words: fetal alcohol spectrum disorders; fetal alcohol syndrome; adopted children; orphanage; developmental delay; ophthalmology

Introduction

Prenatal alcohol exposure may have numerous adverse effects on the fetus, as was discovered in the 1970s by Jones and coauthors (Jones et al., 1973) who coined the term fetal alcohol syndrome (FAS). As more knowledge about the disorder was accumulated, it became clear that the effects fall within a continuum, ranging from subtle disabilities to complete FAS. The term fetal alcohol spectrum disorders (FASD) was introduced to describe the spectrum of structural anomalies and neurocognitive and behavioral disabilities that these children may exhibit (Riley et al., 2011).

Fetal alcohol spectrum disorders are a worldwide problem that has been studied in many countries, such as the United States (Jones et al., 1973), South Africa (May et al., 2013), Russia (Miller et al., 2006), Italy (May et al., 2011), Croatia (Petković and Barisić, 2010), Finland (Autti-Rämö et al., 2006), and Sweden (Olegård et al., 1979; Landgren et al., 2010). In South America, studies on FASD have been performed in Chile (Flanigan et al., 2008; Kuehn et al., 2012), whereas only a few, mostly case studies have been done in Brazil (Silva et al., 1981; Grinfeld et al., 1999; Mesquita and Segre, 2009; Momino et al., 2012), a country with a high consumption of alcohol in certain socioeconomic settings, according to recent reports (Mendoza-Sassi and Béria, 2003; Costa et al., 2004; Gama et al., 2004; Silveira et al., 2012).

Children living in orphanages, including those who have been given up for adoption in various parts of the world, show an increasing number of wide ranging health problems including neurodevelopmental disorders (Albers et al., 1997; Miller et al., 2005, 2006). A meta-analysis on the prevalence of FASD in child care settings, by Lange et al. (2013), reports that these children constitute a population that is high risk for FASD. A study of children who were adopted to Sweden from orphanages in Eastern Europe showed a high frequency of neurodevelopmental deficits; 52% of the children suffered from FASD, with 30% of them having FAS and 51% attention- deficit/ hyperactivity disorder (ADHD) (Landgren et al., 2010). Visual dysfunction and eye anomalies have often been observed in children with FAS (Miller et al., 1981; Strömland, 1987; Strömland and Hellström, 1996; Strömland and Pinazo-Durán, 2002; Grönlund et al., 2004; Ribeiro et al., 2007).

[1]Institute of Neuroscience and Physiology, Department of Ophthalmology, University of Gothenburg, Gothenburg, Sweden
[2]Department of Pediatric Ophthalmology, Altino Ventura Foundation and Hospital de Olhos de Pernambuco, Recife, Brazil
[3]Department of Surgery, Skaraborg Hospital, Skövde, Sweden
[4]Department of Pediatric Neurology, Altino Ventura Foundation, Recife, Brazil
[5]Department of Neuropsychiatry of the Federal University of Pernambuco, Department of Child and Adolescent Psychiatry, Instituto Materno Infantil de Pernambuco and Altino Ventura Foundation, Recife, Brazil
[6]Department of Psychology, Altino Ventura Foundation, Recife, Brazil
[7]Department of Pediatric Surgery, Federal University of Pernambuco, Department of Pediatrics, Altino Ventura Foundation, Recife, Brazil.

Supported by the Altino Ventura Foundation, Recife, Brazil; the Gothenburg Medical Society, Gothenburg, Sweden; and Skaraborg Hospital Research Fund, Skaraborg, Sweden.

*Correspondence to: Kerstin Strömland, Department of Pediatric Ophthalmology, Queen Silvia Children's Hospital, SE 41685 Gothenburg, Sweden.
E-mail kerstin.stromland@vgregion.se

Published online 5 November 2014 in Wiley Online Library (wileyonlinelibrary.com). Doi: 10.1002/bdra.23326

This study focuses on physical and functional deficits and ophthalmological anomalies, with a special focus on FASD, in children staying in an orphanage in Brazil.

Materials and Methods

SUBJECTS

All children living in a specific orphanage in Recife, Brazil, were invited to participate in the study. Altogether 114 children spent some time at the orphanage during the 10 month study period. Ninety-four children (82%) participated, 54 boys and 40 girls aged 3 months to 14 years (mean age, 6.2 years). Several children had one or more siblings staying at the orphanage. Twenty children were excluded. The most common reason for exclusion was that the child left the orphanage before all examinations had been carried out and could not be reached for a complete evaluation. One twin pair was diagnosed with Tay-Sachs disease at the ophthalmological examination and was not further examined. Three children had an adoptive placement before completion of our evaluation. The age of some of the children was estimated, as their birth date was unknown. Some children were anonymously entrusted to the orphanage without further family and/or background information. Most children were from a mixed white and black background. The examinations were performed at the eye hospital of Altino Ventura Foundation, Recife, Pernambuco, Brazil.

METHODS

Information regarding social background, reason for being taken in by the orphanage, health of the child, mother, father, and siblings, alcohol abuse by the mother and father, illicit drugs and tobacco use during pregnancy, and other relevant factors was collected from the health records and through a clinical interview with the staff working at the orphanage. A multidisciplinary team examined the children regarding pediatrics, neurology, psychiatry, psychology, and ophthalmology, using a standard protocol, on 2 separate days. Depending on the neurological and psychological findings, children were referred for neuropsychiatric evaluation.

The Brazilian members of the examining team had no background knowledge of FASD and were therefore unfamiliar with symptoms in children with the disorder. They were trained to recognize its symptoms by one of the authors (K.S.) before the start of the project. They were blinded from any background knowledge at the examination. The guidelines of the Institute of Medicine (IOM) of the National Academy of Sciences, modified by Hoyme et al. (2005), were used for setting out the diagnostic criteria for FASD.

Ninety-four children had a pediatric evaluation. Height, weight, and occipitofrontal circumference (OFC) were measured using an anthropometric digital scale manufactured in Brazil in 2004 (Anthropometric Balmak Model III, São Paulo, SP, Brazil, serial No. 5975) and validated for Brazilian children. Growth deficiency was defined as height or weight $\leq$10th percentile of the reference mean and microcephaly as OFC $\leq$10th percentile of the reference mean. The neurological evaluation included assessment of reflexes and muscle tone, fine and gross motor function, and indicators of the child's general developmental level. Minor facial anomalies characteristic of FASD, including short palpebral fissures ($\leq$10th percentile), smooth philtrum, and thin vermilion border of the upper lip, were assessed. The lip-philtrum guide was used and a score of 4 or 5 was considered pathological (Astley and Clarren, 2000; Hoyme et al., 2005).

Eighty-eight children underwent a neurological examination. A psychological assessment was done in 47 of the 56 children who were 6 years or older. Six children did not show up for the neurological examination, and nine did not appear for the psychological evaluation. Ninety children had a neurological and/or psychological evaluation. Four children were examined by neither the neurologist nor the psychologist. They were evaluated by the pediatrician and the ophthalmologist, who did not find any signs of neurodevelopmental defects. Forty-eight children were referred for a neuropsychiatric evaluation after a primary evaluation by the other members of the examination team.

The psychologist used three tests that have been validated in Brazil: the Wisconsin Card Sorting Test (Cunha et al., 2005), a neuropsychological test of executive functions, focusing on cognitive flexibility and set-shifting, inhibitory control, the Rey Complex Figure Test (Rey and Oliveira, 1999) to test perception and visual spatial memory; and the Raven Colored Progressive Matrices (Special Scale) (Angelini et al., 1999) to evaluate nonverbal intelligence. A child was judged as having a cognitive impairment if he/she had deficits in one or more of the three tests assessing the areas of executive functioning, nonverbal intelligence, and perceptual ability. Deficit was defined as a score of 2 standard deviations or more below average. Structured questionnaires from the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, International Statistical Classification of Diseases and Related Health Problems, 10th revision, and Swanson, Nolan, and Pelham rating scale were used to evaluate ADHD, conduct disorder, oppositional–defiant disorder, obsessive–compulsive disorder, and autism spectrum disorders. The World Health Organization's definition of intellectual disability was applied.

Ninety-four children underwent an ophthalmological evaluation. Based on the child's age and developmental level, a detailed ophthalmological examination was made including measurement of visual acuity, refraction under cycloplegia, strabismus and ocular motility, and examination of anterior and posterior segments of the eye. The face and retinal fundus were photographed. Visual acuity was measured with Snellen chart or using Teller Visual Acuity Cards in children who were $<$3 years old, or had

TABLE 1. *Fetal Alcohol Spectrum Disorders (FASD)[1] in Children Living in the Orphanage (N = 94)*

				Minor physical anomaly				Growth deficiency			Neurodevelopmental deficit		
Diagnosis	Alcohol abuse	Age, yrs	Sex	Palpebrae	Lip	Philtrum	Ophthalmology	Height	Weight	OFC	DD	Cognitive	Behavior
FAS	NA	2.5	M	+	+	+	+	+	+	+	+		
	Mo/Fa	3.8	F	+	+		+	+	+	+	+		
	NA	6.9	F		+	+	+	+	+	+	+	IABA	
pFAS	Mo/Fa	2.5	M	+	+	+				+	+		
	NA	4.9	M		+	+				+			ADHD
	Mo/Fa	5.8	F	+	+			+			+		
	NA	7.0	F	+	+	+						IABA	ADHD
	Mo/Fa	8.1	M		+	+				+			ADHD
	Mo/Fa	8.5	M	+	+	+				+	+	IABA	ADHD
ARND	Mo/Fa	5.1	F	+				+			+		
	Mo/Fa	5.2	M			+						IABA	ADHD, ODD
	Mo	6.1	F	+								IABA	ADHD
	Mo/Fa	6.3	F	+						+		IABA	
	Mo/Fa	6.6	F					+	+		+	IABA	
	Mo/Fa	7.0	M	+							+	IABA	
	Mo	12.8	F					+	+	+		IABA	

According to the diagnostic criteria set out in Hoyme et al., 2005. The table indicates alcohol abuse problems in the mother (Mo) and/or father (Fa) or if no information is available (NA). Lip, thin vermilion border of the upper lip and philtrum, smooth philtrum (score 4 or 5, using the lip–philtrum guide; Astley and Clarren, 2000). Height, weight, and occipital frontal circumference (OFC) $\leq 10^{th}$ percentile are given.

ADHD, attention-deficit/hyperactivity disorder; ARND, alcohol-related neurodevelopmental disorder; DD, developmental delay; FAS, fetal alcohol syndrome; IABA, below average intelligence ability; ODD, oppositional-defiant disorder; Ophthalmology, ophthalmologic findings; Palpebrae, short palpebral fissures $\leq 10^{th}$ percentile; pFAS, partial FAS. The + symbol indicates presence of the anomaly.

poor cooperation, developmental delay or intellectual disability. These children were additionally evaluated regarding their visual behavior and additional ophthalmological signs such as nystagmus, strabismus, and defects of the anterior and posterior parts of the eye. Visual impairment was defined as visual acuity $\leq 20/60$, according to the World Health Organization's definition.

ETHICAL APPROVAL

The study met the requirements established by the Brazilian National Health Council for research in humans, and informed consent was obtained from the directors responsible for the orphanage children.

Results

Data regarding the reason for being taken in by the orphanage, the health of the mother, father, and siblings, and the parents' use of alcohol and drugs were available in 84/94 studied children. The main reasons for being admitted into the orphanage were negligence, child abuse, or abandonment, found in altogether 57 children (61%). Forty-seven children (50%) had mothers who abused alcohol and 35 (37%) had a father with a known alcohol abuse problem. In 33 children (35%), both parents abused alcohol. Eleven children had mothers suffering from mental impairment or psychiatric disease, all combined with alcohol abuse; five of them in addition suffered from drug abuse. In 16 children, both parents had drug abuse problems. One family had four children, all of whom were the result of incest. One mother with two children staying in the orphanage was suffering from AIDS.

One girl had sickle cell anemia. Eighteen children (19%) had growth retardation and 16 (17%) were microcephalic. Growth retardation in combination with microcephaly was found in eight children. Sixteen children (17%) had FASD (Table 1); three (3%) of these had FAS, six (6%)

TABLE 2. *Neurodevelopmental Deficits, Diagnosis in Children, Including Affected Adopted Children, Living in the Orphanage (N = 94)*

Age (yrs)	Sex	DD	ID	Cognitive deficit	Behavioral deficit	FASD	Adopted
2.5	M	+				PFAS	
2.5	M	+				FAS	+
3.1	M	+			ADHD		
3.4	F	+			Autism		
3.8	F	+				FAS	+
4.7	F				ADHD		
4.9	M				ADHD		+
4.9	M				ADHD	pFAS	
4.9	F		+				
5.1	F	+				ARND	+
5.2	M			IABA	ADHD, ODD	ARND	
5.8	F	+				PFAS	+
6.1	F			IABA	ADHD	ARND	
6.3	F			IABA		ARND	
6.3	M			IABA	ADHD		+
6.4	F			IABA			
6.5	M			IABA			
6.6	F			IABA			
6.6	F	+		IABA		ARND	
6.7	M	+					
6.8	M	+		IABA	ADHD		
6.9	F	+		IABA		FAS	
7.0	F			IABA			
7.0	F			IABA	ADHD	PFAS	+
7.0	M	+		IABA			+
7.2	M	+		IABA			+
7.3	M	+					
7.3	M			IABA			
7.8	M	+		IABA			
8.1	M				ADHD	pFAS	+
8.1	M				ADHD		+
8.4	M			IABA			
8.5	M	+		IABA	ADHD	PFAS	
8.8	M			IABA	ADHD		
8.9	M			IABA			
9.2	M			IABA			
9.3	M			IABA			
9.5	M		+		Autism		
9.8	F			IABA			
10.1	M		+		Autism		

TABLE 2. *Continued*

Age (yrs)	Sex	DD	ID	Cognitive deficit	Behavioral deficit	FASD	Adopted
10.4	F				ADHD, ODD		
12.8	F			IABA		ARND	
13.5	F	+					
14.0	F			IABA			

Neurodevelopmental Deficits, Diagnosis in Children, Including Affected Adopted Children, Living in the Orphanage ($N = 94$)

The + symbol indicates presence of developmental delay, intellectual disability, or if the child is adopted.

ADHD, attention deficit hyperactivity disorder; ARND, alcohol-related neurodevelopmental disorder; DD, developmental delay; FAS, fetal alcohol syndrome; FASD, fetal alcohol spectrum disorders; IABA, intellectual ability below average; ID, intellectual disability; ODD, oppositional-defiant disorder; pFAS, partial FAS.

had partial FAS (pFAS), and seven (7%) had alcohol-related neurodevelopmental disorder (ARND). No cases of alcohol-related birth defects were found.

The overall findings showed that 44 (47%) had one or more diagnoses of neurodevelopmental/behavioral and/or cognitive deficits (Table 2). 17 (18%) children were developmentally delayed, three (3%) had intellectual disability, and 25 children (27%) had an intellectual ability below average. ADHD was found in 14 (15%), oppositional–defiant disorder in 2 (2%), and autism in three (3%).

Fifteen (16%) children had one or more ophthalmological findings (Table 3). Visual acuity was measured by Snellen chart in 69 children and by Teller Visual Acuity Cards in the remaining 25. The visual acuity could not be measured in four children. Eight (9%) children were visually impaired. Strabismus was observed in seven percent. One boy had nystagmus. Bilateral optic disk anomalies were found in four children, one of whom had optic nerve hypoplasia and three had large optic nerve heads and enlarged optic cups and pronounced tortuosity of the optic disk vasculature. Major refractive errors were not noted. Three children had FAS, all showing some ophthalmological signs as did the three children who suffered from autism. Eight children with ophthalmological findings had mothers who abused alcohol; three of them were diagnosed with FAS, autism or intellectual disability, while five had an isolated ophthalmological diagnosis.

Twenty-eight children (30%), 18 boys and 10 girls, 3 months to 13 years old (mean age, 6 years) were adopted from the orphanage during the 10-month study period. Six (21%) of these children had FASD; two had FAS, three pFAS, and one had ARND. Eight were developmentally delayed, four had intellectual ability below average, whereas ADHD was found in five of these children (Table 2). The children were adopted inside Brazil (15), to the USA (2), to Italy (7), and to Norway (4).

Discussion

This study was undertaken in Brazil, a developing country with a high proportion of its population living in low socioeconomic conditions. Data on alcohol drinking in Brazil show a pattern of high alcohol consumption with variations by gender, age, marital status, education, and income (Mendoza-Sassi and Béria, 2003; Almeida-Filho et al., 2004; Gama et al., 2004; Kerr-Correa et al. 2005, Laranjeira et al., 2010; Silveira et al., 2012; De Souza et al., 2012; Monteiro, 2013).

To our knowledge, this is one of the first comprehensive studies of children with neurodevelopmental deficits and FASD in Brazil. The trained multidisciplinary team proved to be successful in identifying FASD, which suggests that our approach may be valuable in further research on exposed populations (Jones et al., 2006).

The information about alcohol abuse during pregnancy was uncertain in some mothers; however, where this information was not available, the mother may nevertheless have had high alcohol consumption. This has to be taken into consideration when identifying children with FASD in this population. For FAS and pFAS, the most severe forms of FASD, a confirmed prenatal alcohol exposure is not obligatory, whereas such information is required for the diagnosis of alcohol-related birth defects and ARND (Hoyme et al., 2005; Riley et al., 2011). In view of this, these latter diagnoses may be less definite. It cannot be excluded that some mothers simultaneously abused alcohol and drugs during pregnancy, which may have had an influence on their offspring.

The psychological instruments used in this study were validated for Brazilian conditions and selected to detect cognitive and behavioral deficits typical of FASD. Nearly half of the children had one or more diagnoses of neurodevelopmental/behavioral and/or cognitive deficits, all of which diagnoses were unknown before our examinations. For future studies, it might be desirable to add psychological tests to obtain more information about cognitive and behavioral impairment (Mattson et al., 2013).

An ophthalmological examination is an additional tool in making the diagnosis of FAS, as shown in several reports (Miller et al., 1981; Strömland, 1987; Grönlund

TABLE 3. *Ophthalmological Findings, Known Alcohol Abuse of Parents, and Diagnosis in Children Living in the Orphanage (N = 94)*

Age, yrs	Sex	Ophthalmology	Alcohol abuse	Diagnosis
2.5	M	VI, esotropia, nystagmus, ptosis, optic nerve hypoplasia RL	NA	FAS
3.8	F	Dysmorphic optic nerves with vascular anomalies RL	Mo/Fa	FAS
6.9	F	VA unable, dysmorphic optic nerves with vascular anomalies RL	NA	FAS
3.4	F	VI	NA	Autism
9.5	M	VA unable, exotropia	NA	Autism
10.1	M	esotropia	Mo/Fa	Autism
4.9	F	VI, esotropia	Mo/Fa	ID
1.3	M	VI, dysmorphic optic nerves with vascular anomalies RL	NA	IOD
1.6	M	VI	Mo/Fa	IOD
1.9	F	VI	Mo/Fa	IOD
2.0	F	VI	Mo/Fa	IOD
2.6	F	VI	Mo/Fa	IOD
6.1	M	esotropia	NA	IOD
7.8	F	esotropia	NA	IOD
9.9	F	esotropia	Mo/Fa	IOD

The table indicates alcohol abuse problems in the mother (Mo) and/or father (Fa) or if no information is available (NA).

FAS, fetal alcohol syndrome; ID, intellectual disability; IOD, isolated ophthalmologic diagnosis; L, left; R, right; VA, visual acuity; VA unable, not possible to measure VA; VI, visual impairment.

et al., 2004; Ribeiro et al., 2007). Short palpebral fissures are among the diagnostic criteria for FAS, pFAS, and alcohol-related birth defects (Hoyme et al., 2005). Strabismus and reduced vision are common. Optic nerve malformations, especially optic nerve hypoplasia, are signs of congenital brain damage that may be observed in FAS, and the retinal vessels may show increased tortuosity. The three children with FAS had significant ophthalmological findings (Table 3), whereas no such signs were noted among the children with pFAS or ARND. This is in agreement with previous observations that children with complete FAS often have various ophthalmological findings, whereas the eyes are affected less frequently in milder forms of FASD (Miller et al., 1981; Strömland, 1987; Grönlund et al., 2004; Ribeiro et al., 2007; Flanigan et al., 2008). Seven of the 12 children with another diagnosis than FAS, but who also had an ophthalmological pathology, had parents with alcohol abuse. However, the number of observed subjects is too small to draw a conclusion on the relationship between these ophthalmological findings and alcohol abuse.

When comparing our Brazilian data to data from a study of children adopted from East European orphanages to Sweden (Landgren et al., 2010) we found neurodevelopmental disorders of similar kinds but in a lower number among the Brazilian children. The two studies are not fully comparable as the children who were adopted to Sweden came from many orphanages located in several countries, whereas the Brazilian data originates from only one orphanage and includes all children, both those who remained there and those who were adopted. Moreover, it has to be pointed out that our data should not be considered as representative for all orphanages in Brazil.

Approximately one-third of all children who stayed at the orphanage during the examination period were given up for adoption and many of them had neurodevelopmental impairment. For example, among those suffering from FASD, approximately one third fell into the adoption group.

Nearly half of the children living in the Brazilian orphanage had one or more neurodevelopmental disorders and a considerable number of children were diagnosed with FASD. It is important to target alcohol abuse among pregnant mothers and focus on the devastating effects it might have on their offspring. More than half of the children in our study who had FASD left the orphanage for adoption. Awareness of a possible neurodevelopmental disorder including signs and symptoms of FASD is important in the adoption process. Our observations emphasize the need for further studies of exposed populations in South America. The extent of the problem has to be described to provide appropriate medical, educational, and social support to the children. Prevention activities among high risk women of child-bearing age are an urgent task for the Brazilian society.

Acknowledgments

We thank the board, staff, and volunteers of the Casa Carolina orphanage, Recife; Altino Ventura Foundation for generously letting us use their location, personnel, and equipment for the study; Edilma Silva who recruited the patients and collected psychosocial data on them; and Ana Elisabeth Moura and Andrea Asfora for performing psychological tests on the children.

References

Albers LH, Johnson DE, Hostetter MK, et al. 1997. Health of children adopted from the former Soviet Union and Eastern Europe. Comparison with preadoptive medical records. JAMA 278: 922–924.

Almeida-Filho N, Lessa I, Magalhaes L, et al. 2004. Alcohol drinking patterns by gender, ethnicity, and social class in Bahia, Brazil. Rev Saude Publica 38:45–54.

Angelini AL, Alves ICB, Custódio EM, et al. 1999. Matrizes Progressivas Coloridas de Raven: Escala especial. Manual. São Paulo, SP: Centro Editor de Testes e Pesquisa em Psicologia (CETEPP).

Astley SJ, Clarren SK, 2000. Diagnosing the full spectrum of fetal alcohol-exposed individuals: introducing the 4-digit diagnostic code. Alcohol Alcohol 35:400–410.

Autti-Rämö I, Fagerlund A, Ervalahti N, et al. 2006. Fetal alcohol spectrum disorders in Finland: clinical delineation of 77 older children and adolescents. Am J Med Genet A 140:137–143.

Costa JS, Silveira MF, Gazalle FK, et al. 2004. Heavy alcohol consumption and associated factors: a population-based study. Rev Saude Publica 38:284–291.

Cunha JA, Trentini CM, Argimon IL, et al. 2005. Manual do teste Wisconsin de classificação de cartas. São Paulo: Casa do Psicólogo.

De Souza LH, Dos Santos MC, Oliveira LC, 2012. Padrão do consume de álcool em gestantes atendidas em um hospital publico universitário e fatores de risco associados (Alcohol use pattern in pregnant women cared for in a public university hospital and associated risk factors). [In Portuguese]. Rev Bras Ginecol Obstet 34:296–303.

Flanigan EY, Aros S, Bueno MF, et al. 2008. Eye malformations in children with heavy alcohol exposure in utero. J Pediatr 153: 391–395.

Gama SGN, Szwarcwald CL, Sabroza AR, et al. 2004. Fatores associados à assistência pré-natal precária em uma amostra de puérperas adolescentes em maternidades do Município do Rio de Janeiro, 1999–2000 (Factors associated with precarious prenatal care in a sample of post-partum adolescent mothers in maternity hospitals in Rio de Janeiro, Brazil, 1999–2000). [In Portuguese]. Cad Saude Publica 20(Suppl 1):101–111.

Grinfeld H, Goldenberg S, Segre CA, et al. 1999. Fetal alcohol syndrome in São Paulo, Brazil. Paediatr Perinat Epidemiol 13:496–497.

Grönlund MA, Aring E, Hellström A, et al. 2004. Visual and ocular findings in children adopted from eastern Europe. Br J Ophthalmol 88:1362–1367.

Hoyme HE, May PA, Kalberg WO, et al. 2005. A practical clinical approach to diagnosis of fetal alcohol spectrum disorders: clarification of the 1996 Institute of Medicine criteria. Pediatrics 115: 39–47.

Jones KL, Smith DW, Ulleland CN, et al. 1973. Pattern of malformation in offspring of chronic alcoholic mothers. Lancet 1:1267–1271.

Jones KL, Robinson LK, Bakhireva LN, et al. 2006. Accuracy of the diagnosis of physical features of fetal alcohol syndrome by pediatricians after specialized training. Pediatrics 118:e1734–e1738.

Kerr-Correa F, Hegedus AM, Trincia LA et al. 2005. Differences in drinking patterns between men and women in Brazil. In: Obot IS, Room R, editors. Alcohol, gender and drinking problems - perspectives from low and middle income countries. Geneva: World Health Organisation Department of Mental Health and Substance Abuse. pp. 49–68.

Kuehn D, Aros S, Cassorla F, et al. 2012. A prospective cohort study of the prevalence of growth, facial, and central nervous system abnormalities in children with heavy prenatal alcohol exposure. Alcohol Clin Exp Res 36:1811–1819.

Landgren M, Svensson L, Strömland K, et al. 2010. Prenatal alcohol exposure and neurodevelopmental disorders in children adopted from Eastern Europe. Pediatrics 125:e1178–e1185.

Lange S, Shield K, Rehm J, et al. 2013. Prevalence of fetal alcohol spectrum disorders in child care settings: a meta-analysis. Pediatrics 2013;132:e980–e995.

Laranjeira R, Pinsky I, Sanches M, et al. 2010. Alcohol use patterns among Brazilian adults. Rev Bras Psiquiatr 32:231–241.

Mattson SN, Roesch SC, Glass L, et al. 2013. Further development of a neurobehavioral profile of fetal alcohol spectrum disorders. Alcohol Clin Exp Res 37:517–528.

May PA, Fiorentino D, Coriale G, et al. 2011. Prevalence of children with severe fetal alcohol spectrum disorders in communities near Rome, Italy: new estimated rates are higher than previous estimates. Int J Environ Res Public Health 8:2331–2351.

May PA, Blankenship J, Marais AS, et al. 2013. Approaching the prevalence of the full spectrum of fetal alcohol spectrum disorders in a South African population-based study. Alcohol Clin Exp Res 37:818–830.

Mendoza-Sassi RA, Béria JU, 2003. Prevalence of alcohol use disorders and associated factors: a population based study using AUDIT in southern Brazil. Addiction 98:799–804.

Mesquita MA, Segre CA, 2009. Freqüência dos efeitos do álcool no feto e padrão de consumo de bebidas alcoólicas pelas gestantes de maternidade pública da cidade de São Paulo (Frequency of alcohol effects in fetus and pattern of alcohol consumption by pregnant women at a public hospital in São Paulo city, Brazil). [In Portuguese]. Rev Bras Crescimento Desenvolv Hum 19:63–77.

Miller LC, Chan W, Comfort K, et al. 2005. Health of children adopted from Guatemala: comparison of orphanage and foster care. Pediatrics 115:e710–e717.

Miller LC, Chan W, Litvinova A, et al. 2006. Fetal alcohol spectrum disorders in children residing in Russian orphanages: a phenotypic survey. Alcohol Clin Exp Res 30:531–538.

Miller M, Israel J, Cuttone J, 1981. Fetal alcohol syndrome. J Pediatr Ophthalmol Strabismus 18:6–15.

Momino W, Félix TM, Abeche AM, et al. 2012. Maternal drinking behavior and fetal alcohol spectrum disorders in adolescents

with criminal behavior in southern Brazil. Genet Mol Biol 35; (Suppl):960–965.

Monteiro MG, 2013. Alcohol y Salud Publica en América Latina: ¿cómo impedir un desastre sanitario? (Alcohol and public health in Latin America: how to prevent a health disaster?). [In Spanish]. Adicciones 25:99–105.

Olegård R, Sabel KG, Aronsson M, et al. 1979. Effects on the child of alcohol abuse during pregnancy. Retrospective and prospective studies. Acta Paediatr Scand Suppl 68:112–121.

Petković G, Barisić I, 2010. FAS prevalence in a sample of urban schoolchildren in Croatia. Reprod Toxicol 29:237–241.

Rey A, Oliveira MS, 1999. Teste de cópia e reprodução de memória de figuras geométricas complexas: manual. Adaptação e Padronização Brasileira. v. 1.

Ribeiro IM, Vale PJ, Tenedorio PA, et al. 2007. Ocular manifestations in fetal alcohol syndrome. Eur J Ophthalmol 17:104–109.

Riley EP, Infante MA, Warren KR, 2011. Fetal alcohol spectrum disorders: an overview. Neuropsychol Rev 21:73–80.

Silva VA, Laranjeira RR, Dolnikoff M, et al. 1981. Alcohol consumption during pregnancy and newborn outcome: a study in Brazil. Neurobehav Toxicol Teratol 3:169–172.

Silveira CM, Rosanna Siu E, Wang YP, et al. 2012. Gender differences in drinking patterns and alcohol-related problems in a community sample in São Paulo, Brazil. Clinics 67:205–212.

Strömland K, 1987. Ocular involvement in the fetal alcohol syndrome. Surv Ophthalmol 31:277–284.

Strömland K, Hellström A, 1996. Fetal alcohol syndrome – An ophthalmological and socioeducational prospective study. Pediatrics 97:845–850.

Strömland K, Pinazo-Durán M, 2002. Ophthalmic involvement in the fetal alcohol syndrome: clinical and animal model studies. Alcohol Alcohol 37:2–8.