Maternal Risk Factors for Fetal Alcohol Syndrome and Partial Fetal Alcohol Syndrome in South Africa: A Third Study

Philip A. May, J. Phillip Gossage, Anna-Susan Marais, Loretta S. Hendricks, Cudore L. Snell, Barbara G. Tabachnick, Chandra Stellavato, David G. Buckley, Lesley E. Brooke, and Denis L. Viljoen

Objectives: This is a third exploration of risk factors for the two most severe forms of fetal alcohol spectrum disorders (FASD), fetal alcohol syndrome (FAS) and Partial FAS (PFAS), in a South African community with the highest reported prevalence of FAS in the world.

Methods: In a case control design, interview and collateral data concerning mothers of 72 first grade children with FAS or PFAS are compared with 134 randomly selected maternal controls of children from the same schools.

Results: Significant differences were found between the mothers of FASD children and controls in socio-economic status, educational attainment, and a higher prevalence of FASD among rural residents. The birth order of the index children, gravidity, and still birth were significantly higher among mothers of FASD children. Mothers of children with a FASD are less likely to be married and more likely to have a male partner who drank during the index pregnancy. Current and gestational alcohol use by mothers of FASD children is bingeing on weekends, with no reduction in drinking reported in any trimester in 75 to 90% of the pregnancies that resulted in an FAS child or during 50 to 87% of PFAS-producing pregnancies. There was significantly less drinking among the controls in the second and third trimesters (11 to 14%). Estimated peak blood alcohol concentrations (BAC)s of the mothers of PFAS children range from 0.155 in the first trimester to 0.102 in the third, and for mothers of FAS children the range is from 0.197 to 0.200 to 0.191 in the first, second, and third. Smoking percentage during pregnancy was significantly higher for mothers of FASD children (82 to 84%) than controls (35%); but average quantity smoked is low in the 3 groups at 30 to 41 cigarettes per week. A relatively young average age of the mother at the time of FAS and PFAS births (28.8 and 24.8 years respectively) is not explained by early onset of regular drinking (mean = 20.3 to 20.5 years of age). But the mean years of alcohol consumption is different between groups, 16.3, 10.7, and 12.1 years respectively for mothers of FAS, FASD, and drinking controls. Mothers of FAS and PFAS children were significantly smaller in height and weight than controls at time of interview. The child's total dysmorphology score correlates significantly with mother's weight (−0.46) and BMI (−0.39). Bivariate correlations are significant between the child's dysmorphology and known independent demographic and behavioral maternal risk factors for FASD: higher gravidity and parity; lower education and income; rural residence; drinks consumed daily, weekly, and bingeing during pregnancy; drinking in all trimesters; partner's alcohol consumption during pregnancy; and use of tobacco during pregnancy. Similar significant correlations were also found for most of the above independent maternal risk variables and the child's verbal IQ, non-verbal IQ and behavioral problems.

Conclusions: Maternal data in this population are generally consistent with a spectrum of effects exhibited in the children. Variation within the spectrum links greater alcohol doses with a greater severity of effects among children of older and smaller mothers of lower socio economic status in their later pregnancies. Prevention is needed to address known maternal risk factors for FASD in this population.

Key Words: Fetal Alcohol Syndrome, Partial Fetal Alcohol Syndrome, Fetal Alcohol Spectrum Disorders, Maternal Risk, Alcohol, Pregnancy, South Africa.

From the University of New Mexico (UNM), Center on Alcoholism, Substance Abuse and Addictions (CASAA), USA (PAM), UNM – CASAA (JPG), The University of Cape Town and The Foundation for Alcohol Related Research (FARR), The Republic of South Africa (A-SM), UCT-FARR. (LSH), School of Social Work, Howard University, Washington, D.C., USA (CLS), California State University, Northridge (BGT), UNM-CASAA (CS), UNM-CASAA (DGB), UCT-FARR (LEB), Department of Human Genetics, Faculty of Health Sciences, University of Witwatersrand, National Health Laboratory Service (NHLS), and FARR, The Republic of South Africa (DLV).

Received for publication March 2, 2007; accepted January 8, 2008.

Reprint requests: Philip A. May, UNM-CASAA, 2650 Yale SE, Albuquerque, NM 87106; Fax: (505) 925-2313; E-mail: pmay@unm.edu

DOI: 10.1111/j.1530-0277.2008.00634.x

THE SEARCH FOR specific maternal risk factors for fetal alcohol syndrome (FAS) and all levels of fetal alcohol spectrum disorders (FASD) has been conducted via prenatal clinic (Alvik et al., 2006a,b,c; Bingol et al., 1987; Day et al., 1991, 1993, 1999; Ernhart et al., 1987; Sokol et al., 1986) and epidemiologic studies (Kvigne et al., 2003; May et al., 1983, 2000; Viljoen et al., 2002, 2005). Population-based research is particularly helpful for identifying traits of high risk mothers, and for a comparison with other mothers within a particular geographic region and culture (Alvik et al., 2006c; Kristjanson et al., 2007). In this particular study, we sought a detailed profile of the very highest risk mothers, those who gave birth to children with the most severe FASD, FAS or Partial FAS. Such understanding is particularly useful for approximating the specific and general etiology of FASD in human populations and for formulating prevention strategies to improve public health (Kvigne et al., 2003; May, 1989, 1995; May and Hymbaugh, 1982, 1989).

Alcohol Abuse, Women, and Prenatal Drinking

The general literature on alcohol abuse among females defines heavy drinking women as individuals who: smoke and abuse drugs; cohabitate with alcoholic males; suffer more frequent sexual dysfunction; have alcohol abusing parents; initiated regular drinking at an early age; and have low self-efficacy, poor life goals, and few interests (Baily, 1990; Day et al., 1991; Schlesinger et al., 1990; Shore and Batt, 1991; Shore and Pieri, 1992; Stratton et al., 1996; Wilsnack, 1989, 1991; Wilsnack and Beckman, 1984; Wilsnack et al., 1991). Factors identified as protective from alcohol abuse are: strong normative/cultural support for abstinence or light drinking; high education; religiosity; and unique social, psychological, biological, and genetic traits (Blume, 1990; May et al., 2004; Morse and Weiner, 1996; Viljoen et al., 2001, 2002).

Drinking alcohol heavily and often during pregnancy is the primary risk factor for FASD. But the levels and symptoms of damage in the children emanating from different drinking mothers vary significantly, and this variation is not fully explained by the quantity and frequency of alcohol consumption during pregnancy. Therefore, risk factors other than alcohol exist and serve to mediate, moderate or otherwise alter the effects of alcohol on the fetus (Abel, 1998; Abel and Hannigan, 1995). Multiple co-factors of risk specific to FASD are not as well understood (Hanna et al., 1993; May, 1989; Schmidt et al., 1990). FAS has been associated with: heavy, episodic (binge) drinking that produces high blood alcohol concentrations (BAC); advanced maternal age; high gravidity and parity; unstable marital status; cigarette use; and use of other drugs (Ernhart et al., 1987; Godel et al., 1992; May et al., 1983; Serdula et al., 1991; Sokol et al., 1980; Waterson and Murray-Lyon, 1989). In the United States (U.S.), higher FAS rates are reported among: individuals of low socio-economic status (SES) and low education, those with high scores on various alcohol abuse assessment tools, and females with alcoholic male partners (Abel, 1995; Abel and Hannigan, 1995; Abel and Sokol, 1986; Darrow et al., 1992; Sokol et al., 1986; Stratton et al., 1996). Studies of mothers bearing children with other levels of fetal alcohol spectrum disorder (FASD), referred to by the Institute of Medicine (Stratton et al., 1996) as Partial FAS (PFAS), alcohol-related birth defects (ARBD), and alcohol-related neurodevelopmental deficits (ARND), point to a dose–response effect, although few studies can specify the quantity, frequency, and timing (during the pregnancy) of the dose. Various levels of prenatal alcohol exposure increase the probability of anomalies, such as microcephaly, craniofacial defects, intelligence, and behavioral problems in the offspring (Ernhart et al., 1987; Jacobson et al., 1996; Kodituwakku et al., 2001; Mattson and Riley, 1999; Mattson et al., 1999).

It has been estimated that FAS affects 0.5 to 2.0 per 1,000 children in the U.S. (May and Gossage, 2001) with similar or lower levels in Western Europe (Abel, 1995, 1998). In school studies have estimated the prevalence of FAS to be 3.1 per 1,000 among children in Washington State and 3.7 to 7.4 per 1,000 in Italy (Clarren et al., 2001; May et al., 2006). All levels of FASD have been estimated to affect 1% of the birth population of the U.S. (Sampson et al., 1997), and more recently estimated as 2 to 4% in Italy (May et al., 2006).

One of the problems with researching maternal risk factors for FASD, particularly the most severe levels (FAS and PFAS), has been a low frequency of identifying affected children in clinic settings (Little et al., 1990). Furthermore, the accurate diagnosis of FAS and various other levels of FASD is still debated (Astley, 2006; May and Hoyme, 2007) and has been avoided, for researchers have chosen to utilize general categories of children, such as alcohol exposed/unexposed, when defining maternal risks. Because of the child diagnostic research carried out in schools in the high rate community in South Africa (SA) considered in this paper, there is an excellent opportunity to define maternal risk. FAS and PFAS, have been reported as 46 to 89 per 1,000 in three studies in this community (May et al., 2000, 2007; Viljoen et al., 2005).

The fact that FAS is associated with low SES (Abel, 1995, 1998) is an important and consistent finding regardless of the particular population studied (Bingol et al., 1987; May et al., 2000; Morse and Weiner, 1996; Viljoen et al., 2002). In South Africa, mothers of children with FAS are lower in SES than controls, even though both groups might be classified as low SES elsewhere. One study in the U.S. compared women from differing SES levels who drank 12 drinks daily. Bearing a FAS child was 45 times more common among births to low SES mothers (Bingol et al., 1987).

Prenatal drinking varies among and within populations throughout the world (Abel, 1995, 1998;. In the U.S., England, and Canada, 20 to 32% of pregnant women drink, and in some European countries the rate is higher, sometimes exceeding 50% (Alvik et al., 2006c; Bonati and Fellin, 1991; Centers for Disease Control, 1997; Day et al., 1993; Godel et al., 1992; May, 1989; Primatesta et al., 1993; Serdula et al., 1991; Sokol et al., 1980;

Waterson and Murray-Lyon, 1989). In SA, 34% of urban women and 46 to 51% of small town and rural women report drinking during pregnancy (Croxford and Viljoen, 1998, 1999). Alcohol abuse and FASD cluster in families, evidence that both social and genetic factors influence susceptibility (Kendler et al., 1992; Kvigne et al., 2003; McCaul et al., 1991; Schuckit and Smith, 1996). Some individuals and families appear to escape many symptoms of FASD in spite of substantial alcohol consumption (Abel, 1998; May et al., 1983, 2004; Pierog et al., 1979). Maternal risk involves the interaction of biological, familial, historical, social and psychological influences (Gomberg, 1993).

Background of the Region

This paper presents the results of a third study of maternal risk factors for FASD in a town and its rural areas (population = 45,225, 22% rural) in the Western Cape Province (WCP) of SA. Most people of the region are "Coloured," which in SA denotes racially mixed individuals of African, European, and Asian origin. For those who work in agriculture and wine production, heavy, episodic drinking has existed and is normative among many of the laborers. For several centuries, alcohol was provided daily to farm workers as partial payment for work by a practice called the "Dop." The formal Dop system is now virtually extinct (May et al., 2005, 2007), but the "legacy" of Dop remains among the norms of many subgroups (Crome and Glass, 2000; London, 2000; May et al., 2005; Viljoen et al., 2002). Many local people suffering low pay, limited opportunity, and humble living conditions treat alcohol as a favored commodity, and use it regularly. Episodic drinking is common on weekends. Commercially produced beer and wine are relatively inexpensive and readily available. Many people consume substantial quantities of alcohol over short periods of time (Goodlett and Horn, 2001; Pascoe et al., 1995) producing high BAC's which place a fetus at risk for FASD (Maier and West, 2001; Mattson et al., 2001; Pierce and West, 1986). Alcohol use studies in this region generally focused on males through the late 1990s (Meyers and Parry, 2001; Parry, 2000). Epidemiologic studies of FAS in the region initiated a focus on female drinking (Adnams et al., 2001; May et al., 2000; Viljoen et al., 2002), and the need to identify maternal risk factors for FASD.

METHODS

This case control study compares characteristics of mothers of children with FAS and PFAS with randomly selected control mothers of normal children attending the same schools. This wave of research was initiated in 2002. All first grade children attending public schools, with active consent to participate (81%), were screened for height, weight, and head circumference. Children at or below the 10th centile on height and weight and/or head circumference (n = 306) were advanced further in the diagnostic process. Teams of dysmorphologists, working blinded from the child's history and one another's findings, provided a physical examination for growth, development, and anomalous symptoms. Measurements and symptoms were recorded on a quantified dysmorphology checklist where a high score indicates more features of FASD (Hoyme et al., 2005; May et al., 2007). One hundred of the 108 children suspected of having FAS (8 were lost to follow-up) were administered psychological and life skills tests (Adnams et al., 2001) to assess development. Next, biological mothers of the children suspected of having an FASD were located and interviewed about maternal risks. Finally, a formal case conference on each child reviewed findings on all tests/exams, and final diagnoses were made using revised IOM criteria (Hoyme et al., 2005; Stratton et al., 1996). Fifty-five of the children received a final diagnosis of FAS and 18 received PFAS. The total number of mothers of FASD children who were candidates for this study was, therefore, 73.

Interviews With Mothers of FASD Children

Complete maternal interviews were performed for 57 (78%) mothers of FAS and PFAS children. Collateral information was collected for key variables on the remaining 16 mothers of the children with an FASD. None of the mothers of children with a FASD diagnosis who were alive and contacted refused to be interviewed. As in two previous studies in this region, mothers generally were forthcoming and forthright with information. However, three mothers of FASD children (5.3%) denied using alcohol during the index pregnancy. Four separate, diagnostic, physical exams performed on each of these children by three different dysmorphologists, and psychological and behavioral tests confirmed that a diagnosis of FAS or PFAS was appropriate per IOM guidelines (Hoyme et al., 2005; Stratton et al., 1996) for these three children. Of the 15 mothers not interviewed directly, 3 were deceased and 12 could not be located. Most of the children of the nomadic mothers were in foster, adoptive, or orphanage placement. Information from the 57 mothers interviewed, and collateral information on selected variables from those not interviewed, provided the data for this article. Characteristics of the children of the mothers of FASD children interviewed and those not interviewed are compared in Table 1 as a partial test of whether this sample is representative of all consenting mothers of FASD children in this community.

Controls

All first grade children with consent to participate were eligible for selection as controls, and 150 were selected by strict random methods. Data were collected for 123 control mothers at the same time as other interviews were ongoing. The reasons for no interview of 27 selected control mothers are: 5 of the randomly selected control children were ultimately found to have a FASD, 1 mother was deceased, 6 refused an interview, 12 children were in foster/adoptive placement, and 3 were not located. Some information was obtained via collateral sources on 11 of those not interviewed, leaving a maximum control sample of 134 on some variables. Control children were assessed exactly the same as were all other children. No mothers in the final control group had borne a child with an FASD.

Questionnaire

All mothers were administered identical questionnaires, and all participants received incentive gift baskets of food staples. The questionnaire was developed specifically for the WCP population, it has been pilot tested and refined in studies with over 350 participants (May et al., 2005; Viljoen et al., 2002), and the current version has 240 items. The retrospective collection of information is designed to reconstruct behavior and traits before, during, and after gestation of the index child.

Table 1. Wave 3, Characteristics of Children With FASD and Randomly Selected Control Children Classified by Whether Their Mothers Were Interviewed Versus Mothers Not Interviewed

FASD (n = 72)						Randomly selected controls (n = 142)				
				Significance					Significance	
Child data	Mother interviewed (n = 57) X (SD)	Mother not interviewed (n = 15) X (SD)	P	Alpha = 0.05	Adj. Alpha = 0.007	Mother interviewed (n = 123) X (SD)	Mother not interviewed (n = 19) X (SD)	P	Alpha = 0.05	Adj. Alpha = 0.007
Height centile	4.9 (6.2)	8.4 (7.8)	0.070	[a]	[b]	29.3 (25.5)	21.7 (21.4)	0.216		
Weight centile	3.4 (2.4)	9.4 (10.9)	<0.001			30.4 (25.8)	31.1 (32.3)	0.918		
Occipitofrontal circumference centile	3.8 (4.2)	5.6 (12.4)	0.362			31.9 (26.1)	33.3 (29.8)	0.831		
Verbal IQ[c]	75.4 (11.5)	78.6 (11.9)	0.359			86.5 (13.0)	83.3 (14.9)	0.372		
Nonverbal IQ[d]	77.9 (6.3)	81.6 (7.8)	0.073			85.9 (9.8)	84.0 (10.6)	0.484		
Behavior[e]	12.1 (8.3)	13.5 (8.0)	0.582			6.3 (8.0)	8.1 (7.2)	0.386		
Total dysmorphology score	18.2 (3.4)	18.6 (3.8)	0.664			8.1 (4.2)	7.6 (3.7)	0.645		

[a]or [b]indicates threshold for significance was met.
[c]Tests of the reception of Grammar (TROG).
[d]Raven coloured progressive matrices (Raven).
[e]Personal behavior checklist (PBCL-36).

Even though this was the third study of FASD in this area, stigma about reporting maternal drinking remained lower than in more developed regions. Furthermore, mothers did not know whether their children had an FASD or not at the time of interview. To establish rapport, nonthreatening questions were asked first. Alcohol consumption responses are more accurate in such a format, especially in the context of dietary questions (King, 1994). Respondents were first asked about the health and drinking practices of their relatives and friends. Then the interview moves to information on health, diet and childbearing of the mother. The context, quantity, and frequency of the mother's current drinking are then explored via a 1-week, day-by-day log. Drinks were measured in standard ethanol units: 340 ml can/bottle of beer (5% ethanol), 120 ml of wine (11% ethanol), 95 ml of wine (13.5% ethanol), or 44 ml of distilled spirits (43% ethanol). Respondents viewed pictures of standard containers of local brands to calibrate exact amounts consumed (Kaskutas and Graves, 2000, 2001). Questions on current drinking were used as benchmarks to establish the method of reporting and for refreshing recall before timeline follow-back questions (Sobell et al., 1988, 2001). Then gestational drinking was queried. Some studies have indicated that retrospective postnatal assessment of gestational alcohol use is likely to be more accurate, or at least to provide higher levels of drinking, than that collected in prenatal settings (Alvik et al., 2006a; Czarnecki et al., 1990).

Blood alcohol concentrations (BAC) were estimated via the BACCuS technique (Markham et al., 1993). This computer algorithm is derived from the Rutgers Alco-Calculator (Rutgers University Center of Alcohol Studies, 1983) to calculate standard drinks. One BACCuS program option computed "estimated BAC for a single drinking episode on the basis of the client's gender and weight, the number of standard drinks consumed, and the time taken to consume the drinks" (Markham et al., 1993, p. 420). Peak average BAC for a maternal category is the focus in this study. Because of individual differences in alcohol metabolism, the calculations are "estimations."

Smoking was explored via questions on tobacco purchases and routine practices in this population where most smokers roll their own cigarettes. Respondents were asked about tobacco consumed currently and during pregnancy. One hand-rolled cigarette in SA equals 1 gram of tobacco (May et al., 2000). Other questions inquired about use of other drugs. Body mass index (BMI) was calculated via the metric formula (Molarius et al., 2000): weight in kilograms ÷ (height in meters)^2. Interviews were in Afrikaans, the primary regional language. As is representative of the population in the semi-rural and rural WCP population, over 90% of the participants were Coloured; the remainder were African Blacks and SA Whites.

Data Analysis

Data processing utilized EPI INFO and SPSS to compare groups via two-tailed statistical tests of significance with Bonferroni adjustments to alpha levels that account for familywise error among sets of analyses. In the tables statistical significance is judged using both the standard alpha level of 0.05, and a second column is provided to denote significance at the probability level required by the Bonferroni-adjusted value for the substantive group of interrelated variables analyzed (Tabachnick and Fidell, 2001). The level is calculated by "dividing the acceptable family-wise error rate by the number of comparisons to be made" (Tabachnick and Fidell, 2007, p. 130) in each family of variables, e.g., alcohol use, demographic or smoking in this paper. The text emphasizes results rendered significant by the Bonferroni- adjusted values applied to the probability statistic.

For comparing three groups on continuous variables, one-way Analysis of Variance (ANOVA) was used, with Welch adjustment when homogeneity of variance was significantly violated at alpha = 0.01. Post hoc analyses were utilized to test for

significant differences between each of the three groups via Dunnett-C tests (which compensate for highly different sample sizes and heterogeneity of variance among groups) at an alpha level equivalent, or even more stringent than, to that of the corresponding omnibus ANOVA. (Tabachnick and Fidell, 2007). Only a few post hoc comparisons met significance criteria for a particular adjusted alpha value. These are found in Tables 2 and 5 and are identified by symbols and footnotes.

Pearson correlation coefficients (r) were used in Table 5, and their significance level was determined via F-score values with Bonferroni corrections employed. Because of normality considerations Spearman rho correlations were used for Table 6, also with Bonferroni corrections.

RESULTS

All 57 of the mothers of FASD children that were located alive agreed to an interview. Comparing characteristics of the children of the mothers of FASD children interviewed with the children of those mothers of FASD children not-interviewed (in Table 1), the mean weight centile of the children of interviewed mothers was significantly less at the Bonferroni-adjusted level of $p = 0.007$ or less (3.4 vs. 9.4). None of the other variables was significantly different. There were no significant differences for control mothers interviewed versus not-interviewed. There is little to no difference between children of the interviewed and those not interviewed. More considerations on the representativeness of the sample follows in the discussion section.

Social, Demographic, and Childbearing Data

In Table 2, 7 of the 17 social, demographic, and childbearing variables are significantly different for mothers of FAS vs. PFAS vs. controls using ANOVA at the adjusted level of alpha = 0.007. Age at interview is significantly different among the 3 maternal categories. Rural residence during pregnancy is significantly more common among FAS (71.2%) and PFAS (47.1%) mothers than controls (33.8%). Educational attainment of the mothers forms a significant spectrum where the lowest mean education is among mothers of children with FAS (4.6 years), and highest for controls (8.1) in post hoc analysis as well. Weekly income of the mothers of FAS children is significantly lower (94 Rands or about 15 US Dollars at time of data collection) than controls (211 Rands or about 34 US Dollars).

Gravidity is higher among the FAS mothers, then FASD, and lowest among controls. Birth order data of the index children also forms a spectrum, with FAS children significantly higher at 3.2 than controls at 2.2. Only mothers of FAS children reported a history of stillborn children. Cohabitating when not married also forms a statistically significant spectrum with more of the mothers of FAS children living unmarried with a partner (62%).

Three of the post hoc comparisons were significant ($p < 0.0029$) between the FAS groups and the controls in Table 2, and are indicated by footnotes: education attainment, current income, and birth order of index child.

Alcohol Use in the Extended Families

In Table 3, only 1 of the family drinking variables was significantly different between groups. A greater percentage of the fathers of FASD children drank during the index pregnancy (83 and 75%) than controls (48%). But the quantities of drinks among the drinking fathers, over a 30-day period, do not differ significantly among groups. Similar comparisons were made utilizing only the drinkers in the groups and there were no differences. Therefore, the drinking quantities among drinkers within each group are statistically similar, but the percentage of drinkers within control families is significantly lower than the FASD groups.

Maternal Drinking and Smoking Variables

Significant findings via the ANOVA scores and adjusted alpha levels for drinking variables ($p = 0.0019$) and smoking levels ($p = 0.0045$) for Table 4 are reviewed below. With no significant difference in when women began drinking or drinking regularly, total years drinking at interview approached significance. The current drinker variable formed a statistically significant spectrum with 66% of the mothers of FAS children reporting current drinking, 47% for mothers of PFAS children, and 27% of controls. There has been a substantial reduction in drinking among the mothers of FASD children since giving birth, and the number of drinks consumed in the past week is lower than reported in past community studies. Bingeing still occurs among 26 to 27% of the mothers of the FASD children and 7% of controls. Weekend drinking continues as the predominant pattern among all drinkers.

Women drinkers consume an average of 6.3 to 8.9 drinks per week, and 27 to 57% of the three groups binged in the week before interview, not statistically significant differences. Peak estimated BACs per drinking episode do not differ significantly between the drinkers of the three groups, nor do quantities consumed on weekends. Seventy-three to 100% of all alcohol is consumed on weekends in all three groups, highest among mothers of PFAS children. The standard deviation of the mothers of FAS children is much higher than controls, indicating a larger number of high values in this group. In fact, not presented in Table 4 is that 25.9% of FAS cases currently drink more than the group mean of 7.5, and 21.6% drink 12 or more drinks each week. For controls, 32% of the drinkers have more than 7 drinks per week, but 73% of controls do not drink at all currently.

Before and during pregnancy, mothers of FAS and PFAS children were significantly more likely to drink the same or greater amounts in all trimesters than current use. Compared with their drinking at interview, more mothers of FAS and PFAS children drank at the same level or higher before pregnancy (82 to 80% respectively) than did the controls ($p < 0.001$) and the percentages and significance levels are similar in all trimesters. Levels of consumption prior to pregnancy are 5.7 drinks per drinking day for mothers of FAS

Table 2. Wave 3, Demographic, Socioeconomic and Maternity Variables for Mothers of Children With FAS, Partial FAS, and Randomly Selected Controls

Variable	Mothers of children with FAS (N = 54)[a]	Mothers of children with partial FAS (N = 18)[b]	Control mothers (N = 134)	Test score	p	Significance: Alpha = 0.05	Significance: Adj. alpha = 0.007
Demographic and socioeconomic variables							
Age on day of interview (yr) mean (SD)	37.6 (6.7)	32.3 (5.5)	33.9 (5.8)	7.99	<0.001[c]	[g]	[h]
Residence during index pregnancy (%)							
Rural	71.2	47.1	33.8				
Urban (conventional)	25.0	47.1	63.9				
Urban (informal settlement)	3.8	5.8	2.3	23.45	<0.001[d]	[g]	[h]
Educational Attainment at interview (in yrs) – mean (SD)	4.6 (2.9)[e]	6.5 (2.8)	8.0 (3.1)	22.05	<0.001[c]	[g]	[h]
Church attendance – at interview (%)							
Never or less than once a month	27.7	35.7	24.9				
Often or very often	72.3	64.3	77.2	9.84	0.320[d]		
Frequency of praying – at interview (%)							
Never	2.4	16.7	0.8				
Not very often (<than weekly)	2.4	0.0	3.3				
Often (2–3 times weekly)	4.8	0.0	0.8				
Very often (daily)	90.5	83.3	95.0	15.57	0.016[d]	[g]	
Usual occupation (%)							
Factory worker	1.9	5.9	10.6				
Farm worker	40.4	41.2	19.7				
Office worker	0.0	0.0	3.8				
Housewife	11.5	11.8	20.5				
Domestic (housekeeper, servant)	15.4	0.0	14.4				
Other	13.5	0.0	15.2				
Usually does not work	17.3	41.2	15.9	26.01	0.011[d]	[g]	
Current income (Rands per wk) when working – mean (SD)	94.5 (94.4)[e]	196.3 (369.6)	211.3 (304.1)	7.79[f]	0.001[c]	[g]	[h]
Childbearing variables – (current unless otherwise noted)							
Gravidity – mean (SD)	3.6 (1.6)	3.1 (1.4)	2.9 (1.4)	5.43	0.005[c]	[g]	[h]
Parity, pre- and full term – mean (SD)	3.2 (1.3)	2.9 (1.5)	2.7 (1.2)	3.52	0.031[c]	[g]	
Birth order of index child – mean (SD)	3.2 (1.8)[e]	2.3 (1.2)	2.2 (1.4)	9.04	<0.001[c]	[g]	[h]
Miscarriages – mean (SD)	0.4 (0.7)	0.1 (0.2)	0.2 (0.3)	3.70[f]	0.031[c]	[g]	
Stillborn – mean (SD)	0.1 (0.3)	0.0 (0.0)	0.0 (0.0)	11.32	<0.001[a]	[g]	[h]
Age at birth of the index child – mean (SD)	28.8 (6.4)	24.8 (5.9)	25.7 (5.8)	5.64	0.004[c]	[g]	
Marital status during pregnancy with index child (%)							
Married	18.0	50.0	45.7				
Unmarried, living with partner	62.0	35.7	24.1				
Separated/divorced/widowed	4.0	0.0	0.9				
Single	16.0	14.3	29.3	27.21	<0.001[d]	[g]	[h]

[a]Combines categories of unemployed, not employed because of disability, and not employed and not looking for work.
[b]Data on these variables include both direct interview and collateral information. Any numbers larger than 57 for mothers of FASD children include collateral information.
[c]ANOVA.
[d]χ^2-test.
[e]FAS group significantly different ($p < 0.0029$) from control group in post-hoc comparisons.
[f]Robust test (Welch).
[g]or [h] indicates threshold for significance was met.

Table 3. Wave 3, Reported Current and Past Drinking Practices (at time of interview) of Family and Friends of Mothers of Children With FAS, Partial FAS, and Randomly Selected Controls

Variable	Mothers of children with FAS (n = 37)[a]	Mothers of children with partial FAS (n = 10)[a]	Control mothers (n = 107)[a]	Test score	P	Significance[e] Alpha = 0.05	Significance[e] Adj. alpha = 0.007
Whole sample							
Woman's father							
Drinks consumed over 30 days mean (SD)	285.5 (392.63)	178.1 (215.35)	55.4 (147.55)	3.35[b]	0.068[c]		
Woman's mother							
Drinks consumed over 30 days mean (SD)	188.2 (340.21)	101.1 (198.70)	20.8 (139.83)	3.20[b]	0.063[c]		
Woman's brother							
Drinks consumed over 30 days mean (SD)	207.6 (364.00)	49.4 (100.42)	3.1 (10.39)	3.78[b]	0.047[c]	f	
Woman's sister							
Drinks consumed over 30 days mean (SD)	32.2 (116.29)	21.9 (61.87)	1.6 (6.14)	1.37[b]	0.284[c]		
Woman's best friend							
Drinks consumed over 30 days mean (SD)	35.2 (124.37)	46.3 (102.73)	14.0 (113.83)	0.79	0.459[c]		
Fathers of index child – drank during index pregnancy (%)	82.8	75.0	47.5	11.88	0.003[d]	f	g
Father of index child – drinks consumed over 30 days during pregnancy – mean (SD)	143.6 (219.62)	102.6 (115.05)	70.2 (218.55)	1.27[e]	0.285[c]		
Drinkers only in sample							
Father of index child-drinks consumed over 30 days mean (SD)	173.5 (230.87)	136.8 (113.64)	147.7 (300.37)	0.10	0.918[c]		

[a]Numbers are reduced due to the fact that some respondents did not have living parents or siblings or best friends for which data could be reported.
[b]Robust test (Welch).
[c]ANOVA.
[d]χ^2.
[e]All post hoc comparisons utilizing an adjusted alpha level ($p < 0.0038$) were not significant.
[f] or [g] indicates threshold for significance was met.

children, 3.5 for PFAS mothers and 3.7 for the 27% of control mothers who drank. Estimated peak BAC's between groups approached significance in all trimesters because of bingeing. Overall, bingeing in the index pregnancy is reported by 81% of the mothers of FAS children, 72% of Partial FAS, and 50% of the drinking controls. Estimated peak BAC's during pregnancy range from 0.102 to 0.155 for mothers of PFAS children and 0.191 to 0.200 for mothers of FAS and is most discrepant in the second and third trimesters.

Additional data, not presented in Table 4, indicate that beer was the most favored beverage by mothers of FAS and PFAS children (76 and 100%) for the FAS group (the PFAS mothers are almost exclusively beer drinkers), followed by wine. Four percent of the mothers of FAS children reported having had a problem with alcohol abuse, 24% of mothers of PFAS, and $<1\%$ of controls. There were no significant differences found using an adjusted alpha level ($p = 0.0019$) in any post hoc drinking comparisons.

Smoking is prevalent among all groups. There are no significant differences at alpha = 0.0045 in age when smoking commenced or began on a regular basis. Current smoking prevalence is higher for FASD groups. The mean quantity of tobacco consumed by smokers of all groups is generally quite low, only 30 to 41 cigarettes per week. Quantities smoked are low by U.S. standards and not significantly different among groups. Differential risk lies in the greater proportion of mothers who smoke in the FAS and PFAS groups. Not found in the table, rural residents are more likely to smoke, and most all women "roll their own" which, along with low income, helps keep quantity of use low. Smoking data indicate that a majority of mothers of FAS and PFAS children smoked the same or more during pregnancy than current levels, compared with 24 to 28% of controls. Combining current drinking and smoking, 78% of mothers of FAS children, 81% of mothers of PFAS, and 17% of controls reported *both* smoking and drinking during pregnancy.

All post hoc smoking comparisons utilizing an adjusted alpha level ($p = 0.0043$) were insignificant.

Other Pregnancy Conditions

Additional variables are found in Table 4 that concern stress, physical assault, and treatment for problems with alcohol abuse. No significant differences are found for levels of stress during pregnancy or having received treatment for alcohol abuse. But a significant difference was found between groups for physical assault by husbands. Also mothers of PFAS children are most likely to recognize an alcohol abuse problem.

Maternal Physical Measures

Basic physical measures differ between the three groups (Table 5) with at alpha = 0.0125. Mothers of FAS children

Table 4. Wave 3, Drinking and Smoking Behaviors of Mothers of Children With FAS, Partial FAS, and Randomly Selected Controls

Variable	Mothers of children with FAS (n = 49)[a]	Mothers of children with partial FAS (n = 15)[a]	Control mothers (n = 133)[a]	Test score	P	Significance[e] Alpha = 0.05	Significance[e] Adj. alpha = 0.0019 (drinking) = 0.0045 (smoking)
Drinking history (at time of interview)							
Age first drank alcohol – mean (SD)	18.2 (3.00)	19.5 (2.79)	19.2 (3.70)	1.17	0.314[b]		
Age began drinking regularly – mean (SD)	20.5 (4.15)	20.3 (2.45)	20.8 (4.37)	0.11	0.893[b]		
Total number of years consumed alcohol – mean (SD)	16.3 (7.10)	10.7 (3.95)	12.1 (6.08)	5.85	0.004[b]	g	
Current drinking (at time of interview) – whole sample							
Current drinker (%)[c]	65.9	46.7	26.7	22.22	<0.001[d]	g	h
Current drinks per week – mean (SD)	3.5 (7.69)	1.8 (3.74)	0.8 (4.06)	2.26[e]	0.119[b]		
Binged (3+) one or more days in week preceding interview (%)	25.5	26.7	6.9	13.23	0.001[d]	g	h
Current consumption on weekends – mean (SD)	3.5 (7.40)	1.8 (3.85)	0.8 (3.13)	3.18[e]	0.056[b]		
Percent drinks consume on weekends (%)	100.0	100.0	72.7	2.95	0.229[d]		
Current drinking (at time of interview) – drinkers Only	(n = 29)	(n = 7)	(n = 34)				
Drinks per week – mean (SD)	7.5 (9.90)	6.3 (5.19)	8.9 (8.45)	0.18	0.834[b]		
Binged (3+) one or more days in week preceding interview (%)	41.4	57.1	26.5	3.07	0.215[d]		
Peak BAC (estimated) in week preceding interview – mean (SD)	0.136 (0.119)	0.177 (0.223)	0.165 (0.190)	0.21	0.813[b]		
Drinks consumed on weekends (Fri., Sat., Sun.) – mean (SD)	7.4 (9.50)	6.3 (5.10)	6.5 (6.82)	0.06	0.942[b]		
Drink on weekends (%)	98.7	100.0	73.0	2.86	0.240[d]		
Drinking during the index pregnancy – whole Sample	(n = 50)	(n = 16)	(n = 134)				
Drink month before pregnancy (%)							
Drank about the same (as current use)	18.0	20.0	3.7				
Drank less (than current use)	14.0	0.0	3.7				
Drank more (than current use)	64.0	60.0	17.9				
Did not drink	4.0	20.0	74.6	83.63	<0.001[d]	g	h
Drank during index pregnancy (%)	96.0	93.8	24.8	88.18	<0.001[d]	g	h
First trimester (%)							
About the same (as current use)	75.5	66.7	11.9				
Less (than current use)	6.1	0.0	6.7				
More (than current use)	14.3	20.0	5.2				
Did not drink	4.1	6.7	73.9				
Stopped during trimester	0.0	6.7	2.3	101.56	<0.001[d]	g	h
Second trimester (%)							
About the same (as current use)	78.4	64.3	11.2				
Less (than current use)	5.9	14.3	5.2				
More (than current use)	0.0	0.0	0.7				
Did not drink	5.9	7.1	74.6				
Stopped during trimester	9.8	14.3	8.2	98.80	<0.001[d]	g	h
Third trimester (%)							
About the same (as current use)	70.6	42.9	11.2				
Less (than current use)	5.9	21.4	2.2				
More (than current use)	3.9	7.1	3.0				
Did not drink	5.9	7.1	74.6				
Stopped during trimester	13.7	21.4	9.0	99.31	<0.001[d]	g	h
Drinking Prior to and During the Index Pregnancy – Drinkers only	(n = 43)	(n = 11)	(n = 31)				

Table 4. (Continued)

Variable	Mothers of children with FAS (n = 49)[a]	Mothers of children with partial FAS (n = 15)[a]	Control mothers (n = 133)[a]	Test score	P	Significance[e] Alpha = 0.05	Significance[e] Adj. alpha = 0.0019 (drinking) = 0.0045 (smoking)
Drinks per drinking day prior to pregnancy – mean (SD)	5.7 (4.0)	3.5 (1.4)	3.7 (2.8)	4.28	0.017[b]	g	
Binged 3+ during pregnancy (%)	81.4	72.7	50.0	7.59	0.014[d]	g	
Drinks per drinking day First trimester – mean (SD)	5.7 (3.8)	3.9 (1.4)	3.8 (3.4)	3.10	0.057[b]		
Peak BAC (estimated) first trimester – mean (SD)	0.197 (0.165)	0.155 (0.072)	0.102 (0.112)	3.54	0.034[b]	g	
Drinks per drinking day second trimester – mean (SD)	5.7 (3.7)	3.2 (1.9)	3.7 (3.4)	3.15	0.041[b]	g	
Peak BAC (estimated) second trimester – mean (SD)	0.200 (0.168)	0.124 (0.094)	0.084 (0.092)	4.30	0.018[b]	g	
Drinks per drinking day third trimester – mean (SD)	5.5 (3.9)	2.7 (2.0)	3.7 (3.5)	2.79	0.068[b]		
Peak BAC (estimated) third trimester – mean (SD)	0.191 (0.161)	0.102 (0.117)	0.076 (0.094)	4.20	0.020[b]	g	
Smoking variables – whole sample (at time of interview)	(n = 51)	(n = 17)	(n = 134)				
Age first used tobacco – mean (SD)	16.8 (3.13)	17.8 (5.10)	18.7 (4.46)	2.48	0.089[b]		
Age began smoking regularly – mean (SD)	17.8 (3.76)	18.5 (5.34)	19.3 (4.56)	1.20	0.307[b]		
Current smoker (in last year) (%)	77.6	70.6	35.3	29.09	<0.001[d]	g	h
Current use of tobacco (gm per wk) – mean (SD)	31.7(40.91)	19.5 (21.59)	10.7(19.89)	6.18[1]	0.005[b]	g	
Current use of tobacco - smokers only(gm/wk) – mean (SD)	40.5(42.25)	30.3(19.69)	33.4(21.92)	0.65	0.527[b]		
Pregnancy – whole sample smoking during							
Smoking in months before pregnancy with index child (%)							
Smoked about the same (as current use)	42.0	23.1	15.7				
Smoked less (than current use)	10.0	15.4	8.2				
Smoked more (than current use)	34.0	38.5	12.7				
Did not smoke	14.0	23.1	63.4	46.85	<0.001[d]	g	h
Smoked during index pregnancy (%)	84.3	82.4	35.8	41.66	<0.001[d]	g	h
Smoked in index pregnancy: first trimester (%)							
Smoked about the same (as current use)	58.0	53.3	24.1				
Smoked less (than current use)	10.0	0.0	9.0				
Smoked more (than current use)	16.0	26.7	0.8				
Did not smoke	14.0	20.0	60.9				
Stopped during trimester	2.0	0.0	3.8	56.87	<0.001[d]	g	h
Smoked in index pregnancy: second trimester (%)							
Smoked about the same (as current use)	62.0	53.3	24.1				
Smoked less (than current use)	10.0	0.0	9.0				
Smoked more (than current use)	10.0	20.0	0.0				
Did not smoke	14.0	20.0	62.4				
Stopped during trimester	4.0	6.7	4.5	57.45	<0.001[d]	g	h
Smoked in index pregnancy: third trimester (%)							
Smoked about the same (as current use)	64.0	40.0	23.5				
Smoked less (than current use)	8.0	0.0	9.1				
Smoked more (than current use)	10.0	20.0	0.0				
Did not smoke	14.0	26.7	62.4				
Stopped during trimester	4.0	13.3	4.5	58.12	<0.001[d]	g	h
Drank and smoked during index pregnancy (%)	78.4	81.3	17.9	70.82	<0.001[d]	g	h
Other Pregnancy Variables (at time of interview unless otherwise noted)	(n = 51)	(n = 17)	(n = 132)				
Sources of stress during pregnancy (%)							
Alcohol and substance abuse	19.6	15.4	7.7	5.11	0.078[d]		
Marital problems, relationship	15.2	23.1	10.8	1.96	0.375[d]		
Children/Family	6.5	7.7	6.8	0.02	0.989[d]		
Unemployment, financial	6.5	15.4	7.7	1.12	0.570[d]		

Table 4. (Continued)

Variable	Mothers of children with FAS (n = 49)[a]	Mothers of children with partial FAS (n = 15)[a]	Control mothers (n = 133)[a]	Test score	P	Significance[e] Alpha = 0.05	Adj. alpha = 0.0019 (drinking) = 0.0045 (smoking)
Neighborhood	4.3	0.0	0.8	3.01	0.222[d]		
Problems associated with anger	2.2	0.0	0.8	0.79	0.674[d]		
Health (unplanned pregnancy, etc.)	2.2	0.0	4.6	1.10	0.576[d]		
Other issues	4.3	7.7	3.8	0.43	0.805[d]		
Ever physically assaulted by husband/partner (%)	58.8	60.0	22.5	25.77	<0.001[d]	g	h
Ever had a problem with alcohol abuse (%)	4.3	23.5	0.8[f]	22.91	<0.001[d]	g	h
Ever received treatment for alcohol abuse (%)	0.0	6.7	0.8	5.32	0.070[d]		

[a]Sample size varies throughout this table from one category of data the next because some analyses include drinkers only or in some cases from missing data.
[b]ANOVA
[c]Consumed at least one drink in 12 months preceding interview.
[d]χ^2-test
[e]Robust test (Welch)
[f]All post hoc comparisons between the three groups, using adjusted omnibus drinking or smoking alpha levels, were not statistically different.
[g]or [h] indicates threshold for significance was met.

are lower in weight (54 kg) than mothers of controls (68 kg) in the 3 group ANOVA, and in post hoc analysis. Body mass index (BMI) is also significantly lower for mothers of FAS children than controls.

A significant bivariate negative correlation of the maternal weight provides the highest correlation with the child's dysmorphology score: the lower the mother's weight, the more dysmorphic the child (r = −0.46). The next highest correlations are between BMI and dysmorphology and between maternal height and dysmorphology.

Correlations of Independent Variables With Dysmorphology, IQ, and Behavior

In Table 6 measures of the child's dysmorphology and developmental traits are correlated with maternal risk variables using Spearman's rho with alpha = 004. Age at pregnancy is not significantly associated with dysmorphology score; but all other variables correlate significantly with dysmorphology score. Non-verbal IQ is correlated with all of the variables except age and income. Verbal IQ is correlated with all variables except age, income, gravidity and parity. Behavioral problems, as measured by the personal behavior checklist, correlate significantly with education, rural residence, drinks per day, bingeing during pregnancy, all trimesters of drinking, and tobacco use during pregnancy.

DISCUSSION

Limitations and Strengths of the Study

In a first maternal risk study in SA (Viljoen et al., 2002), 35 of 46 (76%) mothers of children with FAS were located alive (13% were deceased), and 100% of those located agreed to an interview. In a second study (May et al., 2005), 54 of 64 mothers of FAS or PFAS children were located alive and 1 declined participation (83%). In this study, all 57 of the 72 mothers of FASD children who were identified and contacted agreed to be interviewed (79%). Locating and gaining consent from such high numbers of mothers of children with a severe form of FASD are unparalleled in the FASD literature. Working among this particular population is a unique opportunity to capture data on the entire large sample of high risk mothers.

In spite of the very high proportion of mothers interviewed, one could question the representativeness of this sample, suggesting that bias is a possible limitation of this study. One might suggest that smaller women have smaller children and therefore, the sample may be biased by having missed interviews of a few larger women of children with FASD. This would challenge the conclusions about maternal body size and risk for FASD. We have clearly shown in Table 1 that there is little difference (no statistical difference on 13 of 14 comparisons) in the children of those interviewed and those not interviewed in the FASD sample. We have laid these data on the children out clearly so the reader can judge the

Table 5. Wave 3, Current (at time of interview) Anthropometrics for Mothers of Children With FAS, Partial FAS, and Randomly Selected Controls ($n = 175$)

Variable	Mothers of children with FAS	Mothers of children with partial FAS	Control mothers	*F*-Statistic	*P*	Significance: Alpha = 0.05	Significance: Adj. alpha = 0.0125	Correlation with Child's Dysmorphology Score (total sample)	*F*-Statistic	*P*	Significance: Alpha = 0.05	Significance: Adj. alpha = 0.0125
Height, cm mean (SD)	154.7 (5.72)	155.2 (6.72)	157.6 (6.33)	4.17	0.017[a]	c		−0.31	19.48	<0.001	c	d
Weight, kg mean (SD)	53.9[b] (14.88)	56.7 (14.31)	68.3 (17.35)	13.17	<0.001[a]	c	d	−0.46	41.70	<0.001	c	d
Occipitofrontal circumference, cm mean (SD)	54.8 (1.89)	54.9 (2.05)	54.9 (1.75)	0.08	0.922[a]			−0.08	1.25	0.132		
Body mass index mean (SD)	22.5[b] (5.61)	23.5 (5.55)	27.40 (6.89)	10.12	<0.001[a]	c	d	−0.40	33.70	<0.001	c	d

[a]ANOVA.
[b]FAS group mothers significantly different from control group mothers in post hoc analyses using omnibus adjusted alpha levels ($p < 0.0125$).
[c] or [d] indicates threshold for significance was met.

representativeness of the sample for her/himself. We have also presented a similar analysis in a previous study in this community (May et al., 2005). In that study, there was no significant difference in either height or weight of FASD children of those interviewed versus those not interviewed, as well as no difference on 14 of 14 total comparisons. Yet, when the height and weight of those mothers were compared to controls, they were (as in this study) significantly different from the randomly selected maternal controls by both *t*-tests and bi-variate correlation ($p = 0.034$, $r = -0.23$ for height and $p = 0.002$, $r = -24$ for weight). So from at least two studies with two different samples, the height and weight differences between FASD and control mothers in SA are robust in spite of relatively small samples in each study individually.

This study of mothers of diagnosed FAS and PFAS children has other limitations that could influence the quality of data. Data were collected 7 years retrospectively which some have criticized. This long period before data collection was a bigger problem for collateral information than for those interviewed, as collateral information was only available for a few variables on those not interviewed. For mothers interviewed, accuracy of recall may also be a problem in spite of efforts to reconstruct drinking patterns from reports of current daily drinking and locally adapted timeline, follow-back methods. The study population also has limited formal education which may affect the reported drinking data. Additionally, a possible limitation is that the modal drinking pattern is binge drinking which could result in memory loss. But our experience dictates that this is a very candid and honest population with little reason to distort the truth about drinking, as they reside among a highly tolerant or minimally judgmental subgroup of drinkers within SA society where weekend recreational drinking is a major focus of their attention. Also supporting the validity of the methods, is that retrospective reports of alcohol consumption have been found to be as accurate (Robles and Day, 1990) or more accurate (or at least produce reports of higher drinking levels) than prenatal clinic data (Alvik et al., 2006a; Czarnecki et al., 1990; Jacobson et al., 1996). Recent literature supports using day-by-day reporting and reconstruction of drinking histories (Gruenewald et al., 2002; Searles et al., 2002), including reconstructing specifics as detailed as estimated BACs (Carey and Hustad, 2002), and careful calibration through vessels assessment (Kaskutas and Graves, 2000, 2001). We, therefore, began all alcohol reporting with a 7-day current drinking log and by using pictures of standard drink containers. No methods, however, are believed to be as accurate as immediate daily reporting systems of drinking outside of sensitive settings (Searles et al., 2002).

Collecting information on, and assessing gestational drinking, is a highly sensitive issue which affects accuracy in a population, especially those that have high levels of education, general health knowledge, and some specific information on the dangers of prenatal drinking (Alvik et al., 2006a). The questions, sequence, empathic style, and particular follow-back methods used in this study have been refined over the

Table 6. Spearman Correlation Coefficients for Physical Dysmorphology and Three Developmental[a] Measures vs. Selected Traits of Mothers (n = 191)

Trait	Dysmorphology zscore	Developmental traits		
		Verbal IQ[b]	Non-verbal IQ[c]	Behavior[d]
Age at pregnancy	0.13	−0.02	−0.05	0.04
Gravidity	0.23*	−0.18	−0.28*	−0.12
Parity	0.22*	−0.17	−0.30*	−0.14
Education	−0.47*	0.50*	0.50*	0.39*
Income	−0.24*	0.15	0.14	0.10
During pregnancy				
Residence (rural, urban)	0.34*	−0.27*	0.29*	0.29*
Drinks on typical drinking day	0.60*	−0.30*	−0.34*	−0.32*
Drinks weekly	0.70*	−0.32*	−0.38*	−0.34
Binged (3+)	0.45*	−0.25*	−0.28*	−0.32*
Husband/partner's 30 day use of alcohol	0.37*	−0.43*	−0.35*	−0.32
Woman's use of alcohol and tobacco	0.58*	−0.30*	−0.31*	0.36*
Number of drinks consumed weekly during				
First trimester	0.70*	−0.36*	−0.35*	−0.36*
Second trimester	0.67*	−0.32*	−0.27*	−0.32*
Third trimester	0.62*	−0.32*	−0.36*	−0.22*

[a]All scores standardized for age of child at time of testing.
[b]Tests of the reception of grammar (TROG).
[c]Raven colored progressive matrices.
[d]Personal behavior checklist (PBCL36).
*$p < 0.004$; Bonferroni adjusted alpha level for multiple comparisons, $p = 0.004$.

years to produce what we believe are highly accurate data which may be more accurate than is usually obtained in prenatal settings elsewhere (Alvik et al., 2006a; Czarnecki et al., 1990; Jacobson et al., 1996). This population in particular has proven to be quite forthcoming with candid information about drinking. Our experience in this population dictates that (1) the general tolerance of, or support for, heavy weekend binge drinking in this local subculture, (2) a relatively low knowledge level about FAS at the time of pregnancy, and (3) the 6 to 7 year time period that provides opportunity for reflection all contribute to more honest reporting than might have been possible in the prenatal period.

Since all cases studied here have produced a FAS or PFAS child, we have profiled a very high risk group of mothers. Particularly unique are the detailed quantity, frequency, and timing data on drinking among mothers of children with the most severe diagnoses within the spectrum of FASD. Furthermore, because maternal risk is relative and variable between populations (May et al., 2004), it is vital that a control group from the same population was utilized. Absolute levels of alcohol consumption and other risks for FAS births in one population may never provide complete and accurate measures of generalized or absolute risk (e.g., a common human threshold), even though there are many commonalities among risk factor variables (e.g., bingeing) across populations. Our findings are most relevant for SA Coloureds, or people in other developing populations.

Identified Risks for FAS

Some of the general maternal risks that cut across societies have emerged in this study. First, all women studied are of a sub-population in a modernizing society emerging from the repressive policies of apartheid, and all were Coloured or Black. They have fewer social resources than women in more developed populations without a legacy of discrimination; but when compared to controls, mothers of FAS and PFAS children were even lower SES and had fewer social resources. Second, as in other studies, risk for FAS was significantly different between women with higher gravidity and parity, posing greater risk for FASD. Thus, later-borne children are more affected, especially regarding child dysmorphology and non-verbal IQ measures. Third, mothers of FAS and PFAS children were more likely to be cohabitating without being married (Wilsnack, 1989, 1991; Wilsnack and Beckman, 1984; Wilsnack et al., 1991), and had extended families, sexual partners, and friends who drank heavily. Fourth, as illustrated by both case and control group data, in the overall community, frequent, binge drinking is normative among 50% of males, and 7 to 15% of females. Alcohol consumption was much greater for mothers of FAS and PFAS children than for controls in all comparisons, especially regarding rapid binge drinking (see also Khaole et al., 2004). In most every variable of maternal alcohol use and abuse, a spectrum emerged based on the final diagnosis of the child with FAS, PFAS, and control. Alcohol use was greatest in quantity, frequency, and duration among the mothers of FAS children, and generally next most severe among mothers of PFAS children, while lowest among controls. Nevertheless, there are some heavy drinking mothers among controls which raise the question of what a comparison between the children of the heavier drinkers of the three groups would reveal. We intend to explore this in the future as the size of our SA control groups increases from multiple studies. Controls were currently more likely to be abstainers or light drinkers than the mothers of FASD children. Mothers of FASD children

currently practice a significantly more severe drinking pattern and report drinking more heavily throughout the index pregnancy, whereas controls reduce consumption during pregnancy. Fifth, as noted previously (May et al., 2000), SA cases often described particularly acute stressful life events during the index pregnancies as causes of severe prenatal drinking, although the stress measures used in this study were not discriminating among the groups. But physical assault was higher among mothers of FAS and PFAS children. Overall, the most severe life circumstances produce more problem drinking and FASD.

Dop Is Now a Legacy

This study further documents that the formal Dop system is gone. Only 5% of the women of this generation report having received alcohol through Dop in their lifetime, 9.5% of the mothers of FAS and FASD children vs. 3% of controls. Of the mothers of FASD children, 1% received Dop during the index pregnancy, and $< 1\%$ currently received alcohol through Dop. Therefore, the contemporary drinking pattern is most accurately characterized as a "Dop legacy" where alcohol is obtained commercially, rather than the historical, regular issuance of alcohol to laborers. Contrary to the popular conception that wine is the beverage of choice and abuse, beer is the beverage of choice today.

Maternal Age, Nutrition, and Anthropomorphic Considerations

In the previous studies in this community (May et al., 2005; Viljoen et al., 2002), the mean age of mothers at birth of an FAS child was low (26.7 ± 7.6; 28.0 ± 6.4). It was also relatively low in this sample for both FAS and PFAS mothers (27.8 ± 6.0). In the first two studies, the difference in age was not significant between FAS cases and controls. In this study, the difference between FAS, PFAS, and control groups is significant utilizing a single two-tailed ANOVA comparison with no correction (alpha = 0.05) and results approach significance when corrections were made for variance and multiple comparisons. Therefore, the mothers of FAS children are older than either the PFAS or the control group mothers. Age at birth of FAS children in SA is, however, still lower than in most studies in developed countries (Abel, 1998; Jacobson et al., 1996; May et al., 1983), where a significant difference is generally reported between FAS cases, lesser FASD, and controls (Jacobson et al., 1996; Kvigne et al., 2003). This somewhat lower age at birth of an FASD child in SA is rather unique, and is not explained by early age at onset of drinking or drug use in this community. It is explained substantially by duration, degree, and regularity of binge drinking during pregnancy, coupled with other co-factors, such as gravidity and parity as evidenced by the correlation analyses in Table 6.

Also, poor nutrition and small body size may partially explain the low maternal age at birth of children with FAS, the high rates of FASD in this population, and the severity of FAS. Inadequate, life-long and current nutrition, genetic influences, and/or multiple generations of fetal alcohol exposure likely contribute to the high rate of FAS and PFAS. Mothers of FAS and PFAS children were, on average, significantly smaller on two physical measures recorded, weight and BMI; and the correlation measures added significantly lower height as well. Maternal physical traits also correlated negatively with children's dysmorphology scores indicating that smaller mothers who drink have children with more dysmorphology. In drinking trials, in this same study region, smaller, lighter mothers of FAS children (who were not pregnant at the time) produced higher BAC's than heavier, larger controls, partially because they drank faster, but also because they appeared less capable of eliminating alcohol via first pass metabolism (Khaole et al., 2004). These two factors may combine to allow more alcohol to enter the placenta and cause more fetal damage. Conversely, heavier, control mothers produced lower BACs (Khaole et al., 2004).

The exact mechanisms that place the fetuses of smaller, less well-nourished women at higher risk for FASD births have been examined from various perspectives. Women become intoxicated on smaller quantities of alcohol than men (Jones and Jönsson, 1994), because they are smaller and have lower total body water (National Institute on Alcohol Abuse and Alcoholism, 1990, 1997), which is evidenced by higher BACs. Also, diminished activity of gastric mucosal alcohol dehydrogenase (ADH) in women in general and even more so in alcoholic women (Frezza et al., 1990), produces higher BACs. Furthermore, lack of food in the stomach prior to drinking, leads to higher BACs (Jones et al., 1994).

Very recent studies indicate that the combination of undernutrition and alcohol consumption in pregnant, laboratory animals leads to impairment of alcohol metabolism, increased BAC, and decreased maternal growth hormone levels which negatively affect the offspring (Shankar et al., 2006). Fetal weight and liter size is decreased by alcohol-induced undernutrition as well as liter reabsorbtions (Shankar et al., 2006, 2007). Therefore, alcohol-induced fetal growth retardation is potentiated by poor nutrition. In our SA studies we can hypothesize that: the smaller, lighter women who bear the FASD children produce higher BACs because of their slightness and therefore, lower total body water than controls. Also, because of female genetic regulation of ADH (Khaole et al., 2004), and because they have longer histories of heavy drinking which would lead to lower levels of gastric ADH activity (Frezza et al., 1990), they would have higher BACs. Furthermore, the mothers of FASD children would be less likely to be well nourished and to have food in their stomachs when drinking. Mothers of FASD children report being hungry during pregnancy more than controls (17.2 vs. 6.2%). The underweight of some mothers of children with FASD may result from the substitution of calories from alcohol, as this is associated with lower than expected weight among alcohol abusers in other studies (Leiber, 1991). Finally, the interaction of undernutrition, pregnancy, and alcohol lead to decreased

fetal growth and increased structural anomalies, partly through suppressed alcohol metabolism and clearance as in laboratory studies. So in addition to the fact that the mothers of children with FASD drink in binges during the index pregnancies, their slightness, inadequate diet, and length of drinking career may put the fetus at even greater risk via high BACs, and therefore, partially explain the extra ordinarily high rates of FASD in this population.

Moving on to Prevention

Prevention should be formally and actively pursued in the community, particularly in rural areas. Many of the risk factors identified in these studies are amenable to change via social improvement and proven techniques of case management, alcohol treatment, and birth control. New treatment and prevention efforts emphasizing outreach in the highest risk populations of the WCP can be undertaken and guided by this research. Integrating alcohol use into prenatal screening (Bad Heart Bull et al., 1999) in an effort that would also include other major health problems, such as HIV, TB, and alcohol use could be a partial solution (Li et al., 1999), for in the WCP the rate of all three problems is high, each affecting from 7 to 9% of the population (Groenewald, 2002; Republic of South Africa Western Cape Province., 2001). Because of high rates of FASD in this community over time, comprehensive prevention (May, 1995; Stratton et al., 1996) is warranted.

ACKNOWLEDGMENTS

This project was funded by grants RO1AA09440 and UO1AA11685 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the NIH National Center on Minority Health and Health Disparities (NCMHD), and the Foundation for Alcohol Related Research (FARR). Our sincere thanks are extended to Mayor Herman Bailey, the (Western Cape Community) Town Council, Mr. Cecil Driver, Mr. Japie Adams, Mr. Les Arendse, Mr. Hilton Bailey, and each principal of the elementary schools participating in the study. Maggie September, Dickie Naude, Debbie Price, and others from FARR, the University of Cape Town, and the community contributed greatly to the energy and completion of this project. Many individuals from the schools, public health organizations, and the community were indispensable in the research process, including farm owners and operators. The clinical dysmorphology team was headed by Luther K. Robinson, MD. and consisted of Kenneth Lyons Jones, MD, H. Eugene Hoyme, MD, Nathaniel Khaole, MD, and Denis L. Viljoen, MD. Psychological testing of children was directed by Colleen Adnams, MD, Faye Calhoun, DPA, Kenneth R. Warren, PhD, and Ting Kai Li, MD of NIAAA initiated the U.S. collaboration on FAS in South Africa. Their steadfast commitment to the health and welfare of the people of South Africa, and particularly this South African town, their professional consultation, and their support of the South African research since 1996 have been the driving forces of this research.

Protocols and consent forms were approved by The University of New Mexico (Medical School HRRC #96–209, and main campus IRB #9625), the NIH Office of Protection from Research Risks (OPRR), the Ethics Committee of the University of Cape Town, and a local, oversite committee. All mothers providing information actively consented to the study, and each of the mothers or legal guardians provided active consent for their child to participate in the overall study.

REFERENCES

Abel EL (1995) An update on incidence of FAS: FAS is not an equal opportunity birth defect. Neurotoxicol Teratol 17:437–334.

Abel EL (1998) Fetal Alcohol Abuse Syndrome. Plenum Press, New York.

Abel EL, Hannigan JH (1995) Maternal risk factors in Fetal Alcohol syndrome: Provocative and permissive influences. Neurotoxicol Teratol 17:445–465.

Abel EL, Sokol RJ (1986) Maternal and fetal characteristics affecting alcohol's teratogenicity. Neuro-behav Toxicol Teratol 8:329–334.

Adnams CM, Kodituwakku P, Hay A., Molteno CD, Viljoen D, May PA (2001) Patterns of cognitive-motor development in children with fetal alcohol syndrome from a community in South Africa. Alcohol Clin Exp Res 25:557–562.

Alvik A, Haldorsen T, Groholt B, Lindeman R (2006a) Alcohol consumption before and during pregnancy comparing concurrent and retrospective reports. Alcohol Clin Exp Res 30:510–515.

Alvik A, Haldorsen T, Lindeman R (2006b) Alcohol consumption, smoking and breastfeeding in the fist six months after delivery. Acta Pediatr 95:686–693.

Alvik A, Heyerdahl S, Haldorsen T, Lindeman R (2006c) Alcohol use before and during pregnancy: A population-based study. Acta Pediatr 85:1292–1298.

Astley SK (2006) Comparison of the 4-digit diagnostic code and the Hoyme diagnostic guidelines for fetal alcohol spectrum disorders. Pediatrics 118:1532–1545.

Bad Heart Bull LB, Kvigne VL, Leonardson GL, Lacuia L, Welty TK (1999) Validation of a self-administered questionnaire for prenatal alcohol use in Northern Plains Indian women. Am J Preven Med 16(3):240–3.

Baily S (1990) Women with alcohol problems: a psycho-social perspective. Drug Alcohol Rev 9:125–131.

Bingol N, Schuster C, Fuchs M, Iosub S, Turner G, Stone RK, Gromisch DS (1987) The influence of socioeconomic factors on the occurrence of fetal alcohol syndrome. Adv Alcohol Subst Abuse 6:105–118.

Blume SB (1990) Chemical dependence in women: important issues. Am J Drug Alcohol Abuse 16:297–307.

Bonati M, Fellin G (1991) Changes in smoking and drinking behavior before and during pregnancy in Italian mothers: Implications for public health intervention. Int J Epi 20:927–932.

Carey KB, Hustad JTP (2002) Are retrospectively reconstructed blood alcohol concentrations accurate? Preliminary results from a field study J Stud Alcohol 63:762–766.

Centers for Disease Control (1997) Alcohol consumption among pregnant and child-bearing aged women: United States, 1991 and 1995. MMWR 46:346–350.

Clarren SK, Randels SP, Sanderson M, Fineman RM (2001) Screening for fetal alcohol syndrome in primary schools: a feasibility study. Teratology 63:3–10.

Crome IB, Glass Y (2000) The DOP system: A manifestation of social exclusion. A personal commentary on "alcohol consumption amongst South African workers.". Drug Alcohol Depend 59:207–208.

Croxford JA, Viljoen D (1998) Prospective Analysis of Alcohol Ingestion in 636 Pregnant Women in Rural and Urban Areas of the Western Cape. B.S. Medicine University of Cape Town, Dept. of Human Genetics, Cape Town.

Croxford J, Viljoen D (1999) Alcohol consumption by pregnant women in the Western Cape. S Afr Med J 89:962–965.

Czarnecki DM, Russell M, Cooper ML, Salter D (1990) Five-year reliability of self-reported alcohol consumption. J Stud Alcohol 51:68–76.

Darrow SL, Russell M, Cooper ML, Mudar P, Frone MR (1992) Sociodemographic correlates of alcohol consumption among African-American and white women. Women Health 18:35–50.

Day NL, Cottreau CM, Richardson GA (1993) The epidemiology of alcohol, marijuana, and cocaine use among women of childbearing age and pregnant women. Clin Obstet Gynecol 6:232–245.

Day NL, Robles N, Richardson G, Geva D, Taylor P, Scher M, Stoffer D, Cornelius M, Goldschmidt L (1991) The effects of prenatal alcohol use on the growth of children at three years of age. Alcohol: Clin Exp Res 15:67–71.

Day NL, Zuo Y, Richardson GA, Goldschmidt L, Larkby CA, Cornelius MD (1999) Prenatal alcohol use and offspring size at 10 years of age. Alcohol Clin Exp Res 23:863–869.

Ernhart CB, Sokol RJ, Martier S, Moron P, Nadler D, Ager JW, Wolf A (1987) Alcohol teratogenicity in the human: a detailed assessment of specificity, critical period, and threshold. Am J Obstet Gynecol 156:33–39.

Frezza M, Di Padova C, Pozzato G, Terpin M, Baraona E, Lieber CS (1990) High blood alcohol levels in women. The role of decreased gastric alcohol dehydrogenase activity and first-pass metabolism. N Engl J Med 322:95–99.

Godel JC, Pabst HF, Hodges PE, Johnson KE, Foese J, Joffres MR (1992) Smoking and caffeine and alcohol intake during pregnancy in a northern population: effect on fetal growth. Can Med Assoc J 147:181–187.

Gomberg ESL (1993) Women and alcohol: use and abuse. Nerv Ment Diseas 181:211–219.

Goodlett CR, Horn K (2001) Mechanisms of alcohol-induced damage to the developing nervous system. Alcohol ResHealth 25:175–184.

Groenewald P (2002) Annual Report 2000. Boland Overberg Region.. Department of Information Management Worcester, R.S.A.

Gruenewald PJ, Russell M, Light J, Lipton R, Searles J, Johnson F, Trevisan M, Freudenheim J, Muti P, Carosella AM, Nochajski TH (2002) One drink to a lifetime of drinking: Temporal structures of drinking patterns. Alcohol Clin Exp Res 26:916–925.

Hanna EZ, Faden VB, Harford TC (1993) Marriage: does it protect young women from alcoholism? J Subst Abuse 5:1–14.

Hoyme HE, May PA, Kalberg WO, Kodituwakku P, Gossage JP, Trujillo PM, Buckley DG, Miller JH, Aragon AS, Khaole N, Viljoen DL, Jones KL, Robinson LK (2005) A practical clinical approach to diagnosis of fetal alcohol spectrum disorders: clarification of the 1996 institute of medicine criteria. Pediatrics 115:39–47.

Jacobson JL, Jacobson SW, Sokol RJ (1996) Increased vulnerability to alcohol-related birth defects in the offspring of mothers over 30. Alcohol Clin Exp Res 20:356–363.

Jones AW, Jönsson KA (1994) Food-induced lowering of blood-ethanol profiles and increased rate of elimination immediately after a meal. J Forensic Sci 39:1084–1093.

Kaskutas LA, Graves K (2000) An alternative to standard drinks as a measure of alcohol consumption. J Subs Abuse 12:67–78.

Kaskutas LA, Graves K (2001) Pre-pregnancy drinking: how drink size affects risk assessment. Addiction 96:1199–1209.

Kendler KS, Heath AC, Neale MC, Kessler RC, Heath AC, Eaves LJ (1992) population-based twin study of alcoholism in women. JAMA 268:1877–1882.

Khaole NC, Ramchandani VA, Viljoen DL, Li TK (2004) A pilot study of alcohol exposure and pharmacokinetics in women with or without children with fetal alcohol syndrome. Alcohol Alcohol 39:503–508.

King AC (1994) Enhancing the self-report of alcohol consumption in the community: Two questionnaire formats. Am J Pub Health 84:294–296.

Kodituwakku PW, Kalberg W, May PA (2001) The effects of prenatal alcohol exposure on executive functioning. Alcohol Res Health 25:192–198.

Kristjanson AF, wilsnack SC, Zvartau E, Tsoy M, Nivikov B (2007) Alcohol use in pregnant and nonpregnant Russian women. Alcohol Clin Exp Res 31:299–307.

Kvigne VL, Leonardson GR, Borzelleca J, Brock E, Neff-Smith M, Welty TK (2003) Characteristics of mothers who have children with fetal alcohol syndrome or some characteristics of fetal alcohol syndrome. Am Bd Fam Pract 16:296–303.

Lieber CS (1991) Perspectives: Do alcohol calories count? Am J Clin Nutr 54:976–982.

Li C, Olsen Y, Kvigne V, Welty T (1999) Implementation of substance use screening in prenatal clinics. South Dakota Med J 52:59–64.

Little BB, Snell LM, Rosenfeld CR, Gilstrap LC, Gant NF (1990) Failure to recognize fetal alcohol syndrome in newborn infants. Am J Dis Child 144:1142–1146.

London L (2000) Alcohol consumption amongst South African farm workers: A challenge for post-apartheid health sector transformation. Drug Alcohol Depend 59:199–206.

Maier SE, West JR (2001) Drinking patterns and alcohol-related birth defects. Alcohol Res Health 25:168–174.

Markham MR, Miller WR, Arciniega L. (1993) BACCus 2.01: Computer software for quantifying alcohol consumption (A blood alcohol concentration calculating system). Beh Res Meth Instr Comp 25:420–421.

Mattson SN, Goodman AM, Caine C, Delis DC, Riley EP (1999) Executive functioning in children with heavy prenatal alcohol exposure. Alcohol Clin Exp Res 23:1808–1815.

Mattson SN, Riley EP (1999) Implicit and explicit memory functioning in children with heavy prenatal alcohol exposure. J Int Neuropsychol Soc 5:462–471.

Mattson SN, Schoenfeld AM, Riley EP (2001) Teratogenic effects of alcohol on brain and behavior. Alcohol Res Health 25:185–191.

May PA (1989) Research issues in the prevention of fetal alcohol syndrome and alcohol-related birth defects, in Women and Alcohol: Issues for Prevention Research (Howard J, Martin S, Mail P, Hilton M, Taylor E. eds), pp 3293–131. NIAAA, Bethesda, MD.

May PA (1995) A multiple-level, comprehensive approach to the prevention of fetal alcohol syndrome (FAS) and other alcohol-related birth defects (ARBD). Int J Addict 30:1549–1602.

May PA, Brooke L, Gossage JP, Croxford J, Adnams C, Jones KL, Robinson L, Viljoen D (2000) Epidemiology of fetal alcohol syndrome in a South African community in the Western Cape Province. Am J Public Health 90:1905–1912.

May PA, Fiorentino D, Gossage JP, Kalberg WO, Hoyme HE, Robinson LK, Jones KL, Del Campo M, Tarani L, Romeo M, Kodituwakku PW, Deiana L, Buckley D, Ceccanti M (2006) Epidemiology of FASD in a province in Italy: Prevalence and characteristics of children in a random sample of schools. Alcohol Clin Exp Res 30:1562–1575.

May PA, Gossage JP (2001) Estimating the prevalence of fetal alcohol syndrome. A summary. Alcohol Res Health 25:159–167.

May PA, Gossage JP, Brooke LE, Snell CL, Marais A-S, Hendricks LS, Croxford JA, Viljoen DL (2005) Maternal risk factors for fetal alcohol syndrome in the Western Cape province of South Africa: a population-based study. Am J Public Health 95:1190–1199.

May PA, Gossage JP, Marais AS, Adnams CM, Hoyme HE, Jones KL, Robinson LK, Khaole NC, Snell C, Kalberg WO, Hendricks L, Brooke L, Stellavato C, Viljoen DL (2007) The epidemiology of fetal alcohol syndrome and partial FAS in a South African community. Drug Alcohol Depend 88:259–271.

May PA, Gossage JP, White-Country M, Goodhart K, DeCouteau S, Trujillo PM, Kalberg WO, Viljoen DL, Hoyme HE (2004) Alcohol consumption and other maternal risk factors for fetal alcohol syndrome among three distinct samples of women before, during, and after pregnancy: The risk is relative. Sem Med Gen, 127C:10–20.

May PA, Hoyme HE (2007) Response to criticisms raised by Astley to clarifications of the IOM diagnostic criteria for fetal alcohol spectrum disorders (FASD). Pediatrics, online response, in press.

May PA, Hymbaugh KJ (1982) A pilot project on fetal alcohol syndrome among American Indians. Alcohol Health Res World 7:3–9.

May PA, Hymbaugh KJ (1989) A macro-level fetal alcohol syndrome prevention program for Native Americans and Alaska Natives: description and evaluation. J Stud Alcohol 50:508–518.

May PA, Hymbaugh KJ, Aase JM, Samet JM (1983) Epidemiology of fetal alcohol syndrome among American Indians of the Southwest. Soc Biol 30:374–87.

McCaul ME, Turkkan JS, Svikis DS, Bigelow GE (1991) Familial density of alcoholism: effects on psychophysiological responses to ethanol. Alcohol 8:219–222.

Meyers B, Parry CDH (2001) Alcohol use in South Africa, 2001; Medical Research Council of South Africa Fact Sheet. 6:1.

Molarius A, Seidell JC, Sans S, Tuomilehto J, Kuulasmaa K (2000) Educational level, Relative body weight, and changes in their association over 10 years: An international perspective from the WHO Monica Project. Am J Pub Health 90:1260–1268.

Morse BA, Weiner L (1996) Rehabilitation approaches for Fetal Alcohol Syndrome, in Alcohol, Pregnancy, and the Developing Child (Spohr HL, Steinhausen HC eds), pp 249–268. Cambridge University Press, Cambridge, MA.

National Institute on Alcohol Abuse and Alcoholism (1990) Alcohol Alert: Alcohol Metabolism. No. 10 PH 290.

National Institute on Alcohol Abuse and Alcoholism (1997) Alcohol Alert: Alcohol and Women. No. 35 PH 371.

Parry CDH (2000) Alcohol problems in developing countries: Challenges for the new millenium. Suchtmed 2:216–220.

Pascoe JM, Kokotailo PK, Broekhuizen FF (1995) Correlates of multigravida women's binge drinking during pregnancy. A longitudinal study. Arch Pediatr Adolesc Med 149:1325–1329.

Pierce DR, West JR (1986) Blood alcohol concentration: A critical factor for producing fetal alcohol syndrome. Alcohol 3:269–272.

Pierog S, Chandavsu O, Wexler I (1979) The Fetal Alcohol syndrome: some maternal characteristics. Int J Gyn Obstet 16:412–415.

Primatesta P, DelCorno G, Bonazzi MC, Waters WE (1993) Alcohol and pregnancy: An international comparison. J Pub Health Med 15:69–76.

Republic of South Africa Western Cape Province. (2001) Health Status Report. Western Cape Department of Health, Cape Town, S.A.

Robles N, Day NL (1990) Recall of alcohol consumption during pregnancy. J Stud Alcohol 51:403–407.

Rutgers University Center of Alcohol Studies (1983) Alco-Calculator: An Educational Instrument. Alcohol Research Documentation, Inc., Piscataway, NJ.

Sampson PD, Streissguth AP, Bookstein FL, Little RE, Clarren SK, Dehane P (1997) Incidence of fetal alcohol syndrome and prevalence of alcohol-related neurodevelopmental disorder. Teratology 56:317–326.

Schmidt C, Klee L, Ames G (1990) Review and analysis of literature on indicators of women's drinking problems. B J Addiction 85:179–192.

Schlesinger S, Susman M, Koenigsberg J (1990) Self-esteem and purpose of life: a comparative study of women alcoholics. J Alcohol Drug Educ 36:127–141.

Schuckit MA, Smith TL (1996) An 8-year follow-up of 450 sons of alcoholic and control subjects. Arch Gen Psych 53:202–210.

Searles JS, Helzer JE, Rose GL, Badger JG (2002) Concurrent and retrospective reports of alcohol consumption across 30, 90, and 366 days: interactive voice response compared with the timeline follow back. J Stud Alcohol 63:352–362.

Serdula M, Williamson DF, Kendrick JS, Anda F, Byers T (1991) Tends in alcohol consumption by pregnant women: 1985 through 1988. JAMA 265:876–879.

Shankar K, Hidestrand M, Liu X, Xiao R, Skinner CM, Simmen FA, Badger TM, Ronis MJJ (2006) Physiologic and genomic analyses of nutrition-ethanol interactions during gestation: Implications for fetal ethanol toxicity. Exp Biol Med 231:1379–1397.

Shankar K, Ronis MJJ, Badger TM (2007) Effects of pregnancy and nutritional status on alcohol metabolism. Alcohol Res Health 30:55–59.

Shore ER, Batt S (1991) Contextual factors related to the drinking behaviors of American business and professional women. Br J Addict 86:171–176.

Shore ER, Pieri SA (1992) Drinking behaviors of women in four occupational groups. Women Health 19:55–64.

Sobell LC, Agrwal S, Annis H, Ayala-Velasquez H, Echeverria L, Leo GI, Rybakowski JK, Sandahl C, Saunders B, Thomas S, Zioikowski M (2001) Cross-cultural evaluation of two drinking assessment instruments: Alcohol timeline followback and inventory of drinking situations. Subs Use Mis 36:313–331.

Sobell LC, Sobell MB, Leo GI, Cancilla A (1988) Reliability of a timeline method: Assessing normal drinkers' reports of recent drinking and a comparative evaluation across several populations. Br J Addict 83:393–402.

Sokol RJ, Ager J, Martier S, Debanne S, Ernhart C, Kuzma J, Miller SI (1986) Significant determinants of susceptibility to alcohol teratogenicity. Ann NY Acad Sci 477:87–102.

Sokol RJ, Miller SI, Reed G (1980) Alcohol abuse during pregnancy: An epidemiologic Study. Alcohol Clin Exp Res 4:135–145.

Stratton KR, Howe CJ, Battaglia FC eds (1996) Fetal Alcohol Syndrome Diagnosis, Epidemiology, Prevention, and Treatment. National Academy Press, Washington, DC.

Tabachnick BG, Fidell LS (2001) Using Multivariate Statistics (4th ed.). Allynand Bacon, Boston.

Tabachnick BG, Fidell LS (2007) Experimental Designs Using ANOVA. Thomson Brooks/Cole, Belmont, CA.

Viljoen DL, Carr LG, Foroud TM, Brooke L, Ramsay M, Li TK (2001) Alcohol dehydrogenase-2*2 allele is associated with decreased prevalence of fetal alcohol syndrome in the mixed-ancestry population of the Western Cape Province, South Africa. Alcohol Clin Exp Res 25:1719–1722.

Viljoen D, Croxford J, Gossage JP, Kodituwakku PW, May PA (2002) Characteristics of mothers of children with fetal alcohol syndrome in the Western Cape Province of South Africa: a case control study. J Stud Alcohol 63:6–17.

Viljoen DL, Gossage JP, Brooke L, Adnams CM, Jones KL, Robinson LK, Hoyme HE, Snell CL, Khaole N, Kodituwakku P, Asante KO, Findlay R, Quinton BA, Marais AS, Kalberg WO, May PA (2005) Fetal alcohol syndrome epidemiology in a South African community: A second study of a very high prevalence area. J Stud Alcohol 66:593–604.

Waterson EJ, Murray-Lyon IM (1989) Drinking and smoking patterns amongst women attending an antenatal clinic — II during pregnancy. Alcohol Alcohol 24:163–173.

Wilsnack SC (1989) Women at high risk for alcohol abuse. The Counselor: 16–17 & 20.

Wilsnack SC (1991) Sexuality and women's drinking. Alcohol Hlth Res Wrld 15:147–150.

Wilsnack SC, Beckman LJ (1984) Alcohol Problems in Women: Antecedents, Consequences, and Intervention. The Guilford Press, New York.

Wilsnack SC, Klassen AD, Schur BE, Wilsnack RW (1991) Predicting onset and chronicity of women's problem drinking: A five-year longitudinal analysis. Am J Pub Health 81:305–318.