Reproductive Toxicology 46 (2014) 31–39

Contents lists available at ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox

Dietary intake, nutrition, and fetal alcohol spectrum disorders in the Western Cape Province of South Africa

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ARTICLE INFO

Article history:
Received 8 May 2013
Received in revised form 10 January 2014
Accepted 15 February 2014
Available online 22 February 2014

Keywords:
Fetal alcohol spectrum disorders
Dietary intake
Nutrition
Pregnancy and alcohol
South Africa

ABSTRACT

In this study, we describe the nutritional status of women from a South African community with very high rates of fetal alcohol spectrum disorders (FASD). Nutrient intake (24-h recall) of mothers of children with FASD was compared to mothers of normal controls. Nutrient adequacy was assessed using Dietary Reference Intakes (DRIs). More than 50% of all mothers were below the Estimated Average Requirement (EAR) for vitamins A, D, E, and C, thiamin, riboflavin, vitamin B_6, folate, calcium, magnesium, iron, and zinc. Mean intakes were below the Adequate Intake (AI) for vitamin K, potassium, and choline. Mothers of children with FASD reported significantly lower intake of calcium, docosapentaenoic acid (DPA), riboflavin, and choline than controls. Lower intake of multiple key nutrients correlates significantly with heavy drinking. Poor diet quality and multiple nutritional inadequacies coupled with prenatal alcohol exposure may increase the risk for FASD in this population.

1. Introduction

1.1. Nutrition status and alcohol consumption in South African populations

During pregnancy, maternal alcohol consumption and dietary intake may have a profound impact on the health and development of the fetus. Malnutrition, food insecurity, and risky drinking patterns are pervasive in certain segments of the population of South Africa (ZA) [1–10]. Low vitamin A intake, iron deficiency anemia, and stunted growth all represent significant health concerns for ZA [11]. Nutritional inadequacies in school-aged children are common, resulting in underweight (16.8%), wasted (2.5%), and stunted (23.5%) growth [12,13].

Additionally, alcohol use among pregnant women is a major concern. Nearly half (42.8%) of pregnant women surveyed in a Western Cape Province (WCP) study reported drinking alcohol during pregnancy, and over half who drank consumed enough alcohol to place their unborn children at "high risk" for fetal alcohol syndrome (FAS) [7]. The prevalence of fetal alcohol spectrum disorders (FASD) in the Western and Northern Cape Provinces of ZA is among the highest in the world (135.1–207.5 per 1000) [14–18], many times higher than prevalence estimates for the United States and Europe [19].

Alcohol and food absorption are affected by multiple factors including: concurrent consumption, sex, hormones, pregnancy, and/or disease status. While food intake can, in the short term, exert a protective effect from the toxic effects of alcohol consumption [20–22], alcohol consumption over time can adversely affect the quality and quantity of proper nutrient supply and energy intake, particularly for women [23,24]. Dietary intake among heavy drinkers is generally considered poor [25]. A recent study of Ukrainian and Russian mothers found lower mean blood plasma levels for most minerals and significant differences in zinc and copper between drinking mothers and non-drinking mothers [26].

Poor maternal nutrition during the prenatal period can cause low birth weight [27,28]. Dietary intake and alcohol consumption during breastfeeding (median duration 18–24 months in ZA)

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http://dx.doi.org/10.1016/j.reprotox.2014.02.002
0890-6238/

may place newborns at an additional disadvantage due to inadequate delivery of nutrients through breastmilk and exposure to alcohol, a known teratogen [29]. The teratogenic effects of alcohol are increased under certain micronutrient deficiencies such as iron [30], zinc [26], and choline [31,32]. Chronic alcohol use can affect micronutrient absorption and availability [33], but less is known about the effect of binge drinking (sporadic or regular drinking of four or five drinks or more per occasion). However, adequate nutrient intake may partially mitigate the harmful effects of alcohol on fetal development. Vitamin B_3, folic acid, zinc, iron, and choline have all been shown to prevent and/or mitigate some of the effects of prenatal alcohol exposure [30,31,34,35].

1.2. Impetus of this study

In three separate samples in this study community, the body mass index (BMI) of mothers of children with FASD was found to be significantly lower than that of controls, and mothers of children with FASD in most populations have been disproportionally of lower socioeconomic status (SES) [8,9,15,16,18,36]. Dietary intake or other nutrition analyses have not been previously undertaken for mothers of children diagnosed with an FASD. This paper examines dietary and alcohol intake of mothers in a community in the WCP of ZA. Two questions are addressed. First, what proportion of the overall community maternal sample is likely deficient on essential macro and micronutrients? Second, is there a significant difference in dietary intake between mothers of children with FASD and mothers of controls?

2. Methods

2.1. Data collection and instruments

The data in this paper originate from a nested study in a larger epidemiologic inquiry of the prevalence and characteristics of FASD in a community in ZA. A two-tiered process in elementary schools, described fully elsewhere [8,15,18], identified children with FASD and randomly-selected, verified, not-FASD controls. All children in first grade classrooms of all thirteen community primary schools were screened for height, weight, and occipitofrontal head circumference (OFC). All children who were ≤10th centile in height and weight and/or ≤10th centile in OFC and randomly-selected candidates for normal controls received a standardized, comprehensive evaluation, including: (1) independent dysmorphology examinations by at least two dysmorphologists and (2) assessment of IQ, behavioral, and neuropsychological functioning via a battery of eleven tests/scales [37,38]. Biological mothers of children suspected to have an FASD and of the control children were interviewed on maternal risk variables including: use of alcohol at time of interview and during gestation of the index child [8]. Final diagnoses were assigned at a case conference where all findings (child physical, cognitive/behavioral, and maternal risk factors) were reviewed and weighed using revised Institute of Medicine (IOM) criteria [39,40]. If randomly-selected children were found to have an FASD, they were removed from the control group and placed into the FASD group. In this sample, there were 43 children with FASD (24 children diagnosed with FAS, 14 with PFAS (partial fetal alcohol syndrome), and 5 with ARND (alcohol-related neurodevelopmental deficits)) and 85 normal children for comparison.

2.2. Dietary information

Drinking data, current and past, were gathered via a structured interview with the mothers utilizing a time-line, follow-back technique [41,42] to collect multiple measures of drinking. Current drinking questions established a baseline of alcohol use and aid in accurate calibration and recall of drinking. Subsequent questions explored drinking 3 months prior to pregnancy and during each trimester of the index pregnancy. Photographs of the most popular sizes and brands of each type of local alcoholic beverage were used to standardize ethanol units (one standard drink equals 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)) [43,44].

Dietary intake data originate from the maternal risk factor questionnaire and were neither analyzed nor utilized prior to case conference and the assignment of a final diagnosis. Each respondent was queried about food and liquid consumption in a 24-h dietary recall [45,46]. Field interviewers asked detailed questions to ascertain everything each woman drank or ate in the day preceding her interview by portion size, type, preparation, and seasoning. Data were entered into NDSR (version 4.04/32) to obtain estimated nutrient intake for each woman. Having collected baseline information, the interviewer then asked each woman to recall the time of her pregnancy with the index child and to reflect on how her current (preceding day) food and beverage intake was similar to or different from the time of her pregnancy. The 24-h recall method is a commonly used method for dietary surveys. They have been used frequently in African and South African populations [46]. Additional questions assessed the availability of food within the household at the time of that pregnancy.

2.3. Data analysis

Epi-Info software and SPSS were used to input and analyze the data. Chi-square tests were calculated on frequencies for nominal or ordinal-level data, and z-tests and difference of means tests were utilized for interval-level measures to determine difference between study groups. Pearson product-moment correlations were used to determine associations between particular nutrients and alcohol use. Because this is a first exploratory study of nutrition effecting diagnoses of FASD in humans, an alpha level of .05 (two-tailed) was used for determining significance for case control comparison and for correlations, as this study attempted to explore any possible association between nutrition and risk for FASD. Therefore, the alpha of .05 reduces the risk for Type II error (failing to reject a false, null hypothesis), but increases the likelihood of a Type I error (accepting a false, null hypothesis).

Dietary intakes were compared with the Dietary Reference Intakes (DRIs) established by the IOM [47]. The Estimated Average Requirements (EARs) are defined to be an intake that meets the nutritional needs for 50% of individuals in a specific gender and life stage. If there is not sufficient evidence for an EAR to be established, an Adequate Intake (AI) is established. Recommended Dietary Allowance (RDA) is defined to meet the nutritional needs of 97–98% of healthy individuals in a specific gender and life stage. If less than 50% of the sample had nutrient intake below EAR or the mean intake was below AI, we classified the intake to be likely inadequate. If an observed nutrient intake is above the RDA, the observed intake is considered to likely be adequate. Due to extreme variation among individuals of the same sex and ages, and because of the necessity to estimate adequate pregnancy intake from interviews conducted when the subjects were often not pregnant, conclusions about the intake adequacies for nutrient intake between EARs and RDA cannot be easily made [48].

Table 3 represents a link of the post hoc interviews to the index pregnancy. Due to the inter-correlations of energy requirements and energy intake (e.g. higher energy requirements need higher energy intakes), definite conclusions about prevalence of macronutrient adequacy cannot be made. However, the Acceptable Macronutrient Distribution Range (AMDR) indicates a range that provides the essential nutrients for a particular energy source (fats, carbohydrates, protein) yet is associated with reduced risk of chronic diseases [47]. Because U.S. IOM dietary guidelines have been adopted by the South African government, EARs/AIs/AMDRs for pregnant women, aged 19–30, were considered appropriate and used to determine likely inadequacies among this population.

Protocols and consent forms were approved by the University of New Mexico (Medical School HRRC 96-209 and 00-422, 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, single-site assurance committee. All women provided active consent.

3. Results

3.1. Child and maternal characteristics

Detailed demographic, growth, and cognitive/behavioral results for the children in this sample (FASD and controls) have been presented elsewhere [18]. Randomly-selected control children were significantly taller, weighed more, had higher BMIs, larger heads, and much less dysmorphology than those children with FASD. Children with FASD performed significantly lower on verbal and non-verbal IQ tests, and had significantly more problem behaviors.

Maternal data in Table 1 indicate that mothers of children with FASD had significantly lower mean weight and BMI (24.9 vs. 27.3, $p = 0.026$) than did mothers of controls. Mothers of children with FASD were two times more likely to reside in a rural area during the index pregnancy, which generally means lower SES [8,14,48]. On average, mothers of children with FASD had three fewer years of education (5.3 vs. 8.3, $p < .001$). Mothers who had a child with an FASD had higher gravidity, parity, averaged one year older at the birth of the index child, and were more likely to live with a partner, yet were not married ($p = .040$). All alcohol consumption variables in Table 1 are significantly different statistically between maternal groups. Bingeing in the index pregnancy is reported by 67.4% of mothers of children with an FASD and 9.5% of the controls. Mothers of children with FASD were twice as likely to smoke than controls during pregnancy (74–32%). However, smoking in this community is a relatively low quantity behavior; smoking mothers average between 30 and 60 cigarettes per week [8,15,16].

3.2. Dietary intake adequacies

Maternal BMI is a useful indicator of usual adequate energy intake (relative to usual energy expenditure) [47]. BMIs within the normal range ($18.5 < \text{BMI} < 25\ \text{kg/m}^2$) indicate energy intake was adequate for 46.8% of all mothers; 51.6% exceeded requirements. A majority of the macronutrient intakes met or exceeded needs such as: AMDR for total fat (60.9%), carbohydrate (65.6%), and protein (91.4%). But the data suggest that intake of many micronutrients was insufficient (Table 2 and Fig. 1). More than half of all women in this study are likely inadequate (<EAR) for 12 of 15 micronutrients with established EARs. Likely micronutrient deficiencies (greater than 50% of women <EAR) include vitamin A, D, E, C, thiamin, riboflavin, B_6, folate, calcium, magnesium, iron, and zinc. The majority of women likely do not have adequate intakes (<AI) for vitamin K, potassium, choline, omega-3 fatty acids, or fiber. These apparent deficiencies persist even after separation into the maternal groups. Using less stringent nutrient requirements (EARs for non-pregnant females, aged 19–30), more than half of all women are still likely inadequate for seven (vitamin A, D, E, C, folate, calcium, and magnesium) of the 15 micronutrients with EARs (data not shown). Vitamin K, potassium, choline, and fiber still have observed means below AI for non-pregnant females, aged 19–30.

The majority of women are likely adequate on vitamin B_{12} (56.2% >RDA), selenium (71.1% >RDA), and sodium (88.3% >RDA). A limited proportion of the sample is at risk for adverse effects (>Upper Tolerable Limit). While no women exceeded the upper tolerable limit (UL) for selenium (400 ug), 56.2% of mothers exceed the UL for sodium (2.3 g). Vitamin B_{12} does not have an established UL. Conclusions cannot be made about nutrient intakes that fall between EAR and RDA; thus no conclusions about the adequacy of niacin can be made.

Thus far, the results suggest that in our entire sample, there is a generalized inadequate intake for many micronutrients. We next asked whether there are dietary patterns that differentiated mothers of children with FASD from the mothers of the controls. The macronutrient intake patterns did not differ significantly between mothers of children with FASD and controls. Although mothers of children with FASD consumed, on average, less total fat, protein, and cholesterol, this did not reach statistical significance. There is a significant difference in the proportion of mothers who are likely inadequate (<EAR) for certain micronutrients (riboflavin, calcium, and magnesium) such that a greater proportion of mothers of children with an FASD are likely inadequate.

The mean dietary intake of riboflavin, calcium, docosapentanoic acid (DPA), and choline were significantly lower for mothers of children with FASD ($p < .05$) (see Fig. 1). Docosahexanoic acid (DHA) approached significance ($p = .072$), and EPA was also lower for mothers of children with FASD; but statistical significance was not reached at alpha .05 for either of these latter two nutrients or for omega-3 fatty acids overall.

Table 3 presents an assessment of the similarity of the diet at interview with intake during the mother's pregnancy with the index child. It is expected that most women would consume more food during pregnancy, and, within each maternal group, a greater proportion reported consuming more food during the index pregnancy than at the time of the interview. However the proportion of mothers of children with FASD who ate about the same was significantly more than that of controls ($p = .049$), and the population who ate less was significantly higher ($p = .036$) than controls. Less than 2% of the mothers of controls and 3.2% of mothers with children with an FASD reported being hungry or lacking sufficient money for food during their pregnancy, which is not statistically significant.

3.3. Association between maternal dietary intake and alcohol consumption

Table 4 correlations indicate that maternal intake of calcium and riboflavin are significantly, negatively associated with maternal drinking in all trimesters ($r = -.237$ and $r = -.196$), drinks per drinking day ($r = -.252$ and $r = -.179$), bingeing 3 or more drinks per occasion ($r = -.294$ and $r = -.193$), and bingeing 5 or more drinks per occasion ($r = -.225$ and $r = -.230$). Choline, DPA, and DHA were negatively correlated with alcohol consumption, although none of the correlations reached statistical significance. The percentage of calories from saturated fatty acids correlated negatively and significantly with three of five drinking measures.

4. Discussion

4.1. Environmental and nutritional influences on fetal development

The very high prevalence of FASD in this ZA community results from a unique confluence of variables reflecting the effect of drinking on a highly vulnerable population in terms of historic, socioeconomic, and nutritional factors [48–50]. In this study, there

Table 1
Maternal demographic, socioeconomic, childbearing, drinking and smoking variables for by FASD diagnosis.

Variable	Mothers of children with FASD ($n = 43$)	Randomly-selected control mothers ($n = 85$)	*P*
Demographic and socioeconomic variables			
Age on day of interview (yrs) – mean (SD)	35.4 (6.1)	34.4 (6.7)	.574[a]
Height (cm) – mean (SD)	154.5 (6.5)	156.8 (7.6)	.088[a]
Weight (kg) – mean (SD)	59.8 (14.3)	67.7 (15.5)	.006[a]
Body mass index (BMI) – mean (SD)	24.9 (5.5)	27.3 (5.9)	.026[a]
BMI < 18.5 kg/m^2 (%)	4.7	0.0	
18.5 kg/m^2 ≤ BMI ≤ 25.0 kg/m^2 (%)	58.1	40.0	
BMI > 25.0 kg/m^2 (%)	37.2	60.0	.012[b]
Residence during index pregnancy (%)			
Rural	70.0	25.9	
Urban	30.0	74.1	<.001[b]
Educational attainment at interview (in yrs) – mean (SD)	5.3 (3.2)	8.3 (2.4)	<.001[a]
Current monthly income (Rands) – mean (SD)	1613.67 (873)	2433.86 (1830)	.006[a]
Childbearing variables – (current unless otherwise noted)			
Gravidity – mean (SD)	3.6 (1.5)	2.8 (1.1)	.003[a]
Parity, pre- and full term – mean (SD)	3.4 (1.4)	2.7 (1.0)	.005[a]
Birth order of index child – mean (SD)	2.7 (1.5)	2.0 (1.2)	.011[a]
Age at birth of the index child – mean (SD)	27.3 (6.1)	25.8 (6.6)	.243[a]
Marital status during pregnancy with index child (%)			
Married	27.9	30.6	
Unmarried, living with partner	37.2	14.1	
Separated/divorced/widowed	0.0	1.2	
Single	34.9	54.1	.040[b]
Alcohol consumption variables			
Drinking at the time of interview			
Consumed alcohol in preceding week (%)	67.4	20.0	<.001[b]
Binged (3+) one or more days in preceding week (%)	89.7	5.9	<.001[b]
Current # of alcoholic drinks consumed per week – among drinkers – mean (SD)	13.90 (10.41)	4.81 (4.98)	.002[a]
During index pregnancy			
Drank in 1st trimester (%)	90.7	22.4	<.001[b]
Drank in 2nd trimester (%)	90.7	15.3	<.001[b]
Drank in 3rd trimester (%)	88.4	12.9	<.001[b]
Binged (3+) one or more days in during index pregnancy (%)	67.4	9.4	<.001[b]
Binged (5+) one or more days in during index pregnancy (%)	55.8	5.9	<.001[b]
Drinkers per drinking day during index pregnancy – mean (SD)	4.93	0.73	<.001[a]
Tobacco use variables			
Smoked during index pregnancy (%)	74.4	31.8	<.001[a]
Smoked and consumed alcohol during index pregnancy (%)	67.4	15.5	<.001[a]
Smoked and binged (3+) during index pregnancy (%)	55.8	7.1	<.001[b]
Smoked and binged (5+) during index pregnancy (%)	48.8	4.7	<.001[b]

[a] *t*-Test.
[b] χ^2 Test.

were significant differences in demographic and socioeconomic variables, and nutritional intake that all appear to negatively impact fetal development over and above the effects of alcohol intake by mothers.

The majority of women were likely inadequate (<EAR) on most nutrients and not meeting DRI. The majority of all women were likely deficient on vitamin A, D, E, K, C, thiamin, riboflavin, vitamin B_6, total folate, calcium, magnesium, iron, zinc, potassium, and choline. Researchers have demonstrated that nutritional deficiencies in pregnant animals can lead to altered morphology, physiology, and performance in offspring [51]. Deficiencies in these nutrients can negatively impact acute and chronic diseases in infants and children. Suboptimal or marginal nutrient intakes observed in this sample are not typically associated with overt disease, but the overall nutrient intake of these mothers is likely a contributing factor to poor fetal development in the presence of a known teratogen, alcohol. Furthermore, inadequacy of specific vitamin intake among the group of mothers bearing children with FASD may invite and justify further inquiry into any specific association or role they may play in the development of traits of FASD, both physical and cognitive/behavioral.

Calcium was most deficient among mothers of children with FASD, and it plays a vital role in bone formation, neurotransmitter release, gene expression regulation, and signaling processes. When maternal dietary calcium intake is low, fetal bone development and mineralization may be compromised [52]. Furthermore, both chronic and acute alcohol consumption reduce circulating osteocalcin, a protein that interacts with calcium and is required for bone formation. Early clinical studies of FAS indicated that bone age was deficient in children with many severe cases of FAS [53].

Omega-3 fatty acids during pregnancy are essential for development of neural tissue and visual function. Although there are no DRI for these individual omega-3 fatty acids, the IOM recommends that about 10% of total omega-3 intake should come from DPA and EPA [54]. For pregnant women, this equates to about 0.14 g/day, and the intake of mothers of children with FASD in this ZA sample is far below the IOM recommendation for DPA and EPA. Omega-3 fatty acid intakes are believed to be most critical during the last trimester of pregnancy and the first few months of life when rapid accretion occurs in the central nervous system. The lack of omega-3's directly and adversely affects fetal brain development and cognitive function later in life [55,56]. DHA is particularly important in cognitive development [57,58], and a recent study suggests that supplementation with DHA improves birth weight and gestation duration [59]. EPA also shows promise as a bioactive nutrient to promote brain development and function [60], and its mechanisms

Table 2
Comparison of nutrient intake to dietary reference intake among women of children with an FASD and controls, Western Cape Province, South Africa.

Nutrient	EAR[a]/AI[b]	All women (n = 128)			Mothers of children with FASD (n = 43)			Mothers of control children (n = 85)			Significant difference of FASD and controls
		Mean	SD	% less than EAR[d]	Mean	SD	% less than EAR[d]	Mean	SD	% less than EAR[d]	
Total grams	NA	1729	(502)	–	1699	(355)	–	1744	(563)	–	.580
Energy (kcal)	NA	1476	(449)	–	1454	(335)	–	1488	(499)	–	.645
Total fat (g)	NA	51	(32)	–	48	(24)	–	53	(36)	–	.478
Total carbohydrate (g)	135	204	(61)	–	206	(39)	–	203	(70)	–	.819
Total protein (g)	50	52	(19)	–	50	(17)	–	53	(20)	–	.417
Cholesterol (mg)	≤300[c]	213	(167)	–	197	(133)		221	(183)	–	.444
Dietary fiber (g)	28	13.4	(5.4)	–	14.4	(5.12)		12.9	(5.4)	–	.148
Vitamin A (retinol equiv) (mcg)	550	639	(934)	66.4	510	(466)	67.4	705	(1095)	65.9	.162
Vitamin D (mcg)	10	2.1	(1.9)	99.8	1.7	(1.5)	100	2.2	(2.0)	98.8	.106
Vitamin E (mg)	12	3.6	(3.3)	97.7	3.4	(2.4)	97.7	3.7	(3.7)	97.6	.544
Vitamin K (mcg)	90	55	(128)	–	43	(38)	–	61	(154)	–	.317
Vitamin C (mg)	70	52	(50)	77.3	54	(41)	74.4	50	(54)	78.8	.642
Thiamin (mg)	1.2	1.16	(.35)	59.4	1.1	(.22)	65.1	1.18	(.40)	56.5	.461
Riboflavin (mg)	1.2	1.09	(.55)	70.3	0.97	(.31)	86.0	1.16	(.63)	62.4	.024
Niacin (mg)	14	15.37	(5.4)	46.1	15.2	(5.12)	46.5	15.47	(5.56)	45.9	.773
Vitamin B_6 (mg)	1.6	1.2	(.48)	77.3	1.2	(.45)	76.7	1.22	(.50)	77.6	.718
Total Folate (mcg)	520	247	(135)	96.4	246	(95)	97.7	247	(151)	96.5	.959
Vitamin B_{12} (mcg)	2.2	3.6	(4.8)	37.5	3.2	(2.8)	32.6	3.7	(5.6)	40.0	.500
Calcium (mg)	800	362	(165)	96.1	305	(83)	100	392	(187)	94.1	<.001
Magnesium (mg)	290	196	(57)	95.3	197	(43)	100	196	(64)	92.9	.912
Iron (mg)	22	9.7	(3.6)	98.4	9.7	(3.0)	100	9.7	(3.9)	97.6	.924
Zinc (mg)	9.5	7.4	(3.1)	76.6	7.7	(3.0)	74.4	7.4	(3.2)	77.6	.617
Selenium (mcg)	49	85	(43)	14.1	77	(28)	9.3	89	(48)	16.5	.094
Sodium (mg)	1500	2736	(1565)	–	2920	(1685)	–	2644	(1502)	–	.368
Potassium (mg)	4700	1951	(645)	–	1983	(553)	–	1935	(691)	–	.671
Choline (mg)	450	255.4	(115.5)	–	239.4	(82.0)	–	271.1	(140.7)	–	.048
Omega-3 fatty acids (g)	1.4	1.2	(0.67)	–	1.3	(0.5)	–	1.2	(0.8)	–	.812
Eicosapentanoic acid (EPA) (g)	NA	0.038	(.094)	–	0.02	(.05)	–	0.05	(.11)	–	.101
Docosapentanoic acid (DPA) (g)	NA	0.01	(.02)	–	0.006	(.01)	–	0.014	(.03)	–	.021
Docosahexanoic acid (DHA) (g)	NA	0.06	(.11)	–	0.04	(.06)	–	0.07	(.13)	–	.072

[a] Estimated Average Requirement (EAR) for pregnant women, aged 19–30, used for: carbohydrate, protein, vitamin A, C, D, E, thiamin, riboflavin, niacin, vitamin B_6, folate, vitamin B_{12}, calcium, magnesium, iron, zinc, and selenium.
[b] Adequate Intake (AI) for pregnant women, aged 19–30, used for dietary fiber, vitamin K, sodium, potassium, choline, and omega-3 fatty acids.
[c] IOM recommends cholesterol intake to be "as Low As Possible while consuming a nutritionally adequate diet". Less than 300 mg per day is recommended by USDA.
[d] Percentage less than EAR is not reported for nutrients where the Institute of Medicine deemed there is insufficient evidence to establish an EAR.

of action on various developmental processes mirror those of DHA [61,62]. Much less is known about the biological function of DPA, and given the very low intake of DPA in mothers of children with FASD, understanding the biological significance of this finding is important.

Low levels of riboflavin intake in mothers of children with FASD are problematic for energy production and development, as riboflavin is needed to convert vitamin B_6 and folate into useable forms. Vitamin B_6 plays a role in certain gene expressions and neurotransmitter synthesis (serotonin, epinephrine, norepinephrine, and gamma-Aminobutyric acid). While, folate is a major requirement for brain and spinal cord development as well as regulation of gene expressions specifically by silencing certain sequences, riboflavin also plays a role in brain development [63–65].

Choline intake, also significantly lower in mothers of children with FASD, serves as an essential nutrient required for most cellular

Table 3
Comparison of dietary intake at time of index pregnancy to current intake for women who gave birth to children with an FASD and randomly-selected controls.

Variable	Mothers of Children with FASD (n = 43)	Control mothers (n = 85)	Difference in proportions test result (z-score)	p
Similarity of diet on day of interview compared to time of pregnancy				
Ate about the same (%)	19.4	35.2	1.97	.049
Ate less (%)	38.7	20.4	2.10	.036
Ate more (%)	41.9	44.4	0.27	.789
Often hungry during pregnancy? – (% Yes)	3.2	1.8	0.45	.649
One reason there was insufficient food in home during pregnancy – (% Yes)				
Not enough money	3.1	0.0	1.16	.246
No transportation to shops	0.0	0.0	–	–
Other reasons	0.0	3.8	1.82	.069

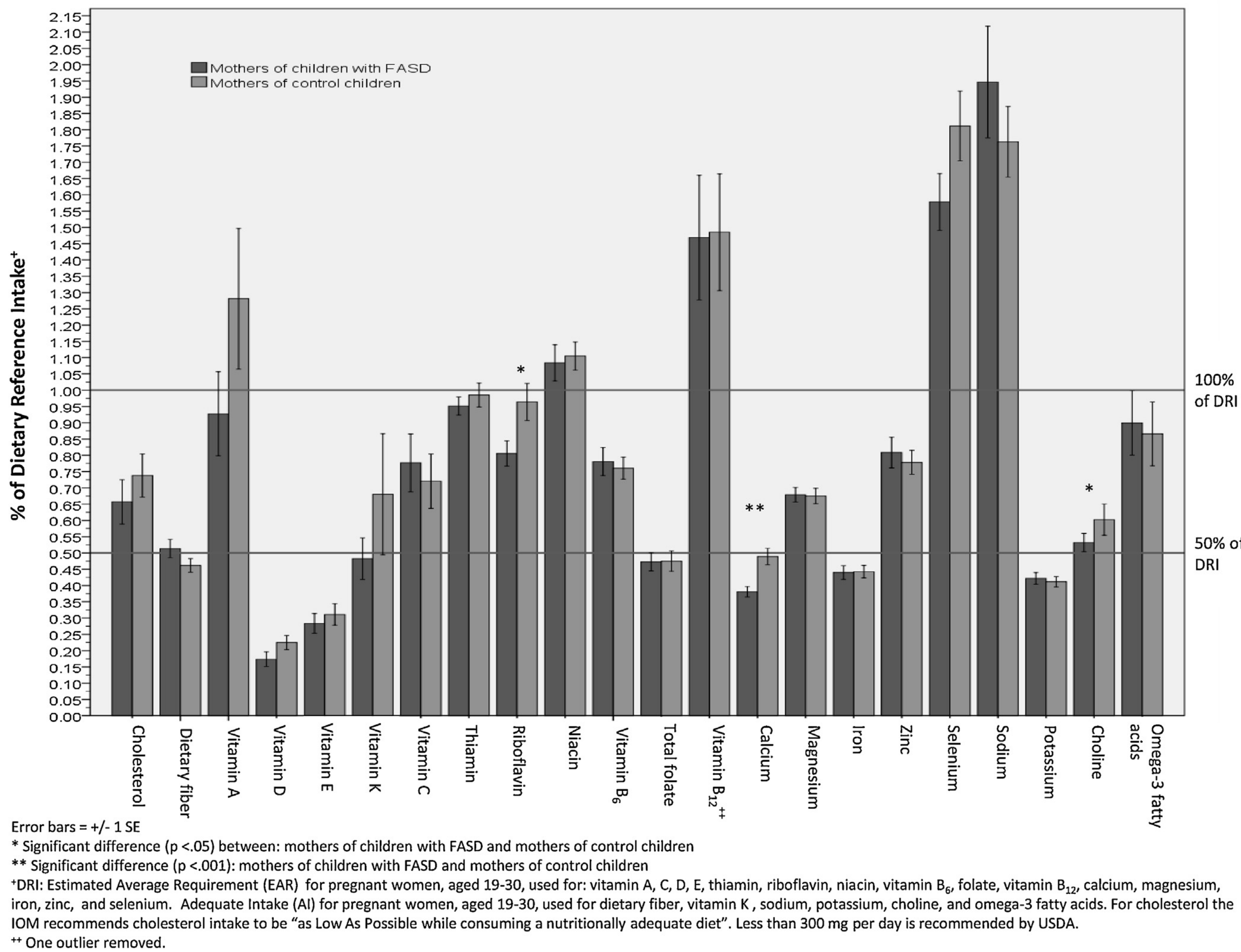

Fig. 1. Percentage of Dietary Reference Intake (DRI) of essential nutrition of mothers of children with FASD and controls from a community in South Africa.

functions [66]. Choline deficiency during pregnancy and lactation may cause deficient motor function and memory in the offspring [32,51]. Multiple lines of evidence point toward a critical role of choline in brain development and cognition [67].

The majority of women were likely consuming adequate amounts of vitamin B_{12} and selenium. While the mean intake of vitamin B_{12} and selenium are higher than reported elsewhere [68,69], dietary staples in South Africa have been shown to be high in selenium [70]. While 56.2% mothers exceed the UL for sodium (2.3 g) and are at risk for adverse effects, the mean intake is below the typical US diet (~4000 mg/day).

4.2. *Alcohol complicates the nutrition scenario*

Alcohol passes freely across the placental barrier. Deficient nutritional status and alcohol interact, thus compounding the independent teratogenic effect of alcohol [71,72]. In addition to alcohol's influence on bioavailability of nutrients, drinking measures in this sample were associated with overall decreased nutrient intake for multiple nutrients, particularly with calcium, riboflavin, and percent of calories from saturated fatty acids (SFA). With patterns of heavy episodic (binge) drinking being the most harmful to the fetus [8–10,36,73,74], lighter (lower BMI) women from this

Table 4
Pearson product-moment correlation coefficients of specific maternal nutrient intake deficiencies[a] with alcohol use and smoking.

	Drank in all trimesters	Drinks per drinking day	Binge 3+ drinks per occasion	Binge 5+ drinks per occasion	Drank and Smoked During Pregnancy
Riboflavin	−.196*	−.179*	−.193*	−.230*	−.203*
Calcium	−.237**	−.252**	−.294**	−.225*	−.171
Choline	−.078	−.131	−.096	−.094	.014
DPA	−.014	.138	−.054	.004	−.057
DHA	.008	.073	−.072	−.009	−.012
% of calories from SFA	−.082	−.211*	−.214*	−.184*	−.085

* $p \leq .05$.
** $p \leq 01$.
[a] Only those nutrients that were statistically significantly different in Table 2 were included with the exception of DHA which approached significances and the measure of percentage of calories from saturated fatty acids (SFA).

exact community population who binge drink have been shown to be less able to eliminate alcohol via first-pass metabolism allowing more alcohol to cross the placenta [75]. Conversely, in heavier mothers the additional adipose tissue helps distribute the alcohol, and therefore, protects the fetus. The rate of alcohol metabolism is also much slower in the fetus causing the alcohol to remain in the fetal body and amniotic fluid longer than in the mother. In animal models, undernutrition and alcohol consumption lead to impaired ability to metabolize alcohol, increased Blood Alcohol Concentration (BAC), and decreased maternal growth hormone levels, all of which negatively impact the offspring [71]. Therefore, it is likely that alcohol-induced fetal growth retardation is potentiated by inadequate nutrient intake and smaller body size.

4.3. Limitations

The major limitation of this study is that dietary intake information was not collected in the prenatal period of the index child, but for a 24-h period seven years later. Although our questions attempted to link the data to the pregnancy, the change in diet over the years and problems of recall to the time of pregnancy could negatively impact the study. Underreporting is common with 24-h dietary recalls, as participants have imperfect memory of consumption. On the other hand, time-line, follow back alcohol inventories are robust in their accuracy for many years [76,77]. Given the individual variation, determining adequacy is not precise; however, the nutrient intakes were analyzed as outlined by the IOM recommendations for DRI [47,78]. Furthermore, the small sample of children with an FASD makes it difficult to generalize these findings. But the overall findings indicate that most women in this community are deficient on intake of many micronutrients. Also the data associating nutrient intake with drinking measures and low BMI with the likelihood of a birth of a child with FASD are provocative.

A second limitation is that adequate diets, better living conditions, more stimulating conditions, and cessation of drinking may combine, both prenatally and postpartum, for better child outcomes in ways that we cannot fully understand from these types of analyses. While individual-level environmental conditions have been associated with an FASD birth outcome [49,50], changing these conditions in the short-term is difficult, over time an improvement in social conditions may result in improved birth outcomes. It should also be noted that the data were collected prior to the ZA food fortification legislation implemented in October 2003. However, an evaluation of the pre-fortification and post-fortification micronutrient intake of ZA women found that >70% of lactating women did not meet the EAR for fortified nutrients: zinc, vitamin A, riboflavin, or B_6 and >80% had inadequate intakes for non-fortified nutrients: calcium, vitamin B_{12}, C, and D [65]. Others have found similar post-fortification deficiencies [68]. This suggests that monitoring the micronutrient status of women of childbearing age should be a public health priority not only to help improve the outcome of alcohol-exposed pregnancies, but also to improve general population outcomes.

A third limitation is a lack of blood samples that could have been used to validate the findings of the 24-h dietary recall. This study used only the NDSR database to estimate the nutritional composition of South African foods. While it is common to use US-developed nutrient software to estimate micronutrient composition of foods, and South African health officials have adopted US standards, some bias may have been introduced by using an American database in this particular South African context. Blood analysis would also allow for more definitive conclusions regarding maternal nutrient deficiencies. But, given the high proportion of mothers who were below EAR, it is likely that the mothers are truly deficient and potentially the children may also have been deficient.

5. Conclusions

The dietary intake profile and nutritional deficiencies in this sample are consistent with other studies in ZA. The proportion of women likely deficient on most micronutrients suggests nutritional interventions are warranted for women of childbearing age. While better living and more stimulating conditions in a majority of households in this community will be difficult to change in a short period of time, better diets and nutritional supplementation can be achieved quite quickly. These approaches may be promising for public health prevention and intervention to minimize FASD in ZA and in other populations of the world.

Conflict of interest

The authors declare that there are no conflicts of interest.

Transparency document

The Transparency document associated with this article can be found in the online version.

Acknowledgements

Funding was provided by the NIAAA (RO1 AA09440, UO1 AA11685, and RO1/U01 AA 015134), the National Center on Minority Health Disparities (NCMHD), and the Foundation for Alcohol Related Research (FARR). We thank the women who provided the information for this study. We are also indebted to Denis Viljoen and Chris Shaw of FARR and to Loretta Hendricks, Leana Marais, and Dicky Naude who participated in the collection of the data. We also thank University of New Mexico student employees Jason Buchan, Eileen Estrada, Matthew Hernandez, Gloria King, Megan Malavoz, Cindy Michelman, Gwyneth Moya, Robert Newcomb, Ethel Nicdao, Jenny Romero, and Audrey Solimon who assisted with data entry. David Buckley assisted in preparing this manuscript. Jason Blankenship participated in the data management, statistical analysis, and preparation of this manuscript prior to his untimely death on October 29, 2013.

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