Published in final edited form as:

Reprod Toxicol. 2016 January ; 59: 101–108. doi:10.1016/j.reprotox.2015.11.006.

MATERNAL NUTRITIONAL STATUS AS A CONTRIBUTING FACTOR FOR THE RISK OF FETAL ALCOHOL SPECTRUM DISORDERS

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Abstract

Objective—Compare nutritional status of 57 South African mothers of children with fetal alcohol spectrum disorders (FASD) with 148 mothers of controls.

Methods—Dietary data were analyzed for macronutrients, micronutrients, and fats via Estimated Average Requirements (EAR) and Adequate Intakes (AI) for pregnant women.

Results—Virtually all mothers were likely deficient on most micronutrients by either EAR (<50%) or AI values. Mothers of FASD children consumed more of 13 of 25 micronutrients. For percentage below EAR, only vitamin D was significantly higher for FASD mothers. Despite no difference in total food intake, control mothers had a higher mean body mass index (BMI) than FASD mothers. Maternal BMI is more significant for positive child outcomes than any individual nutrient.

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Conclusions—Most mothers have inadequate dietary intake. Minor advantages in nutrient intake are overpowered by teratogenic effects of alcohol. Further study is needed of the interaction of alcohol, maternal nutrition, and metabolism.

1. INTRODUCTION

Several epidemiologic studies have analyzed the association between alcohol consumption and nutrient intake. Alcohol abuse is associated with a higher risk for nutrient deficiencies including iron, zinc, copper, folic acid, thiamin (B₁), riboflavin (B₂), vitamin B₆, vitamin C, and vitamin A [1–3]. Alcohol consumption can lead to nutrient deficiencies by affecting nutrient availability through: replacement of nutrients (e.g., a person who drinks more, may eat less) or interfering with the gastrointestinal absorption of the nutrients, particularly for proteins and vitamins. Diet quality has also been shown to be worse for individuals who drank high quantities with low frequency (binge) than individuals who drank low quantities with high frequency [4].

In South Africa (ZA), malnutrition is pervasive in certain segments of the population. Food poverty, where a household does not acquire enough food to maintain an adequate diet, was reported among 43% of ZA households [5–7], with sustained insecurity and income poverty contributing to inadequate nutrient intake across ZA [8]. Despite limited disposable incomes, many women in ZA engage in recreational, weekend binge drinking with 34% of urban and 46–51% of rural women reporting drinking during pregnancy [9]. When maternal nutritional status is compromised by the presence of alcohol, essential nutrients are unavailable for the fetus which can result in suboptimal outcomes such as physical abnormalities, cognitive delays, or fetal alcohol syndrome (FAS), the most severe type of fetal alcohol spectrum disorders (FASD) [10]. The prevalence of FASD in ZA ranges from 135.1–207.5 per 1,000, the highest reported rate of FASD in a general population the world, and many times higher than the United States and Europe [11]. Previous studies have demonstrated that specific nutrient deficits (iron, copper, and choline) were linked to slow growth trajectories or other criteria of FASD [3,12].

In four separate samples in this study community, the body mass index (BMI) of mothers of children with FASD was found to be significantly lower than controls [11,13–16]. Drinking trials conducted in this same region indicated that smaller, lighter mothers of children with FAS (not pregnant at the time) produced higher blood alcohol concentrations (BAC) than heavier, larger controls. This is partially due to the FAS mothers consuming the alcohol more quickly, but also because they appeared less capable of eliminating alcohol via first pass metabolism [17]. These factors may allow additional alcohol to cross the placenta and into the fetus to cause additional fetal damage [17].

This manuscript represents the second study of dietary intake of mothers with children with FASD in this community with an entirely different sample. In the previous study, nearly all women in the sample were significantly below the Dietary Reference Intakes (DRI) and lower intake of multiple nutrients correlated significantly with heavy drinking, poor performance of offspring on cognitive and behavioral measures, and key physical features of

FASD [18]. The current paper aims to determine further the role nutrition as a distal risk factor for FASD in the Western Cape Province of ZA.

2. METHODS

The data presented here originate from an epidemiologic inquiry of the prevalence and characteristics of FASD in a community in ZA. The in-school, active case ascertainment process, described more fully elsewhere [13,14,16], identified children with FASD and randomly-selected, not-FASD controls. All children in first grade were screened for height, weight, and occipitalfrontal (head) circumference (OFC). Children < 10th centile on height and weight and/or OFC and all randomly-selected control candidates received identical evaluations, including a brief dysmorphology exam and cognitive and behavioral assessments. Then biological mothers of children suspected to have FASD and mothers of randomly-selected controls were interviewed on variety of maternal demographic, childbearing history, and alcohol consumption risk factors.

Nutrition data originated from the maternal risk factor questionnaire and was collected via a 24-hour dietary recall [19]. The interviewer asked detailed questions to ascertain everything a woman ate or drank in the preceding day by portion size, type of food, preparation, and seasoning. The interviewer then asked each woman to recall her pregnancy with the index child and consider how her food and beverage intake was similar to that of her pregnancy. Drinking data were gathered using a time-line follow-back technique [20,21] with photographs of popular alcoholic beverages by brands and sizes to standardize ethanol units by quantity, frequency, and timing of use [22,23].

2.1 Sample

The sample includes 57 mothers of children diagnosed with one of the two specific FASD diagnoses: 45 with FAS, 12 with partial fetal alcohol syndrome (PFAS), and 148 normal, control children, 42 of whom were exposed to alcohol prenatally and 106 were not. Children are from the same community in ZA and attended the same schools. Nearly all subjects are mixed-race (“Coloured”) individuals.

2.2 Data analysis

Maternal and child data were entered using Epi Info software [24] and analyses performed with SPSS [25]. Dietary intake data were analyzed using Nutritional Data System for Research (NDSR) version 2014 [26], developed by the Nutrition Coordinating Center at the University of Minnesota. As defined by the Institute of Medicine (IOM), the Estimated Average Requirement (EAR) represents an intake that meets the nutritional needs for 50% of a specific gender and life stage [27]. If there are insufficient data to establish an EAR, an Adequate Intake (AI) is established. Recommended Dietary Allowance (RDA) meets the nutritional needs of 97–98% of healthy individuals in a specific gender and life stage. If half of the sample was below EAR or the mean intake was below AI, for this study, we classified the intake as likely inadequate [27]. Conclusions about nutrient intake adequacy that fall between EAR and RDA cannot be easily determined, but are considered likely sub-optimal [27]. Due to inter-correlations of energy requirements and energy intake, definitive

conclusions about macronutrient adequacy cannot be made. The Dietary Recommended Intake (DRI), for pregnant women, aged 19–30, were used in comparison analyses.

Chi-square tests were calculated on variables that involved data with nominal or ordinal level measurement. Difference of means tests (t-tests and one-way ANOVAs) were utilized for testing statistically significant differences with interval level data. Pearson product-moment correlations were used to determine associations between specific nutrients, BMI, and child outcomes. To determine the role of nutrition in risk for FASD, an alpha level of .05 (two-tailed) was used for case control comparison and correlations.

3. RESULTS

Child growth and cognitive/behavioral measures for children with FASD and controls are presented in Table 1. Only the sex ratio was similar across groups. Nine of the ten analyses are statistically significant: randomly-selected control children were younger, taller, weighed more, and had higher BMI, larger heads, and much less dysmorphology than those children with FASD. On most physical traits, the alcohol-exposed control means fell in the intermediate range between FASD and unexposed controls: height, weight, head circumference, and mean dysmorphology score were all higher than the children with FASD and lower than the unexposed controls. Children with FASD performed significantly lower on verbal and non-verbal IQ tests and had significantly more teacher-reported problem behaviors than controls.

In Table 2, the mothers of children with FASD were lighter, shorter, lower BMI, higher gravidity, had fewer years of education, lower income, and tended to live in more rural areas than controls. Mothers of children with FASD had the fewest mean years of education (5.0 years). Residing in rural areas, which in this region generally indicates lower SES, is significantly more common (71.4%) among mothers of children with FASD. Weekly income was significantly lower for mothers of children with FASD (421.5 Rand, less than \$60 USD at the time of the study) than exposed control mothers (698.9 Rand, <\$120 USD) and unexposed (772.8 Rand, <\$130 USD). Mothers of children with FASD drank significantly more drinks per drinking day and drinks per week during all trimesters than did mothers of exposed controls. In post-hoc, Dunnett C comparisons, maternal weight and all pregnancy drinking measures significantly differentiate all the maternal groups from one another. Also height, BMI, income, gravidity, and still births are significantly different between the FASD group and the unexposed controls. Maternal BMI indicates the usual adequate energy intake, relative to usual energy expenditure, with $18.5 < \text{BMI} < 26 \text{ kg/m}^2$ considered to be adequate intake [27]. Based on this measure, mothers of children with FASD and mothers of exposed control children in the sample had adequate energy intake, while mothers of unexposed children exceeded requirement. However, the nutrient-level data below suggest that micronutrient intake was insufficient for the majority of the women.

Analyses of the 24-hour dietary recall are presented in Tables 3 and 4. In Table 3 the mean intake for all women in this sample was below EAR/AI for all nutrients except total carbohydrates, riboflavin, niacin, vitamin B₁₂, phosphorus, selenium, and sodium. In most cases, the deficits were statistically significant between the three maternal groups, the mean

dietary intake values were significantly different for: vitamin D, C, thiamin, pantothenic acid, B₁₂, phosphorus, magnesium, selenium, sodium, potassium, eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA) (see Table 3). Six additional nutrients (energy, total protein, vitamin E, niacin, choline, and omega-3 fatty acids) approached significance. Mothers who had children with FASD consumed, on average, a significantly greater quantity of 13 macro- and micronutrients compared to control mothers. Post-hoc analyses indicate a statistically significant difference between mothers of children with FASD and unexposed controls in: vitamin D, thiamin, phosphorus, selenium, sodium, EPA, DPA, and DHA. Between mothers of children with FASD and exposed controls, there is a significant difference in: vitamin C, selenium, and EPA. There is no significant pairwise difference between group means of mothers of exposed and unexposed controls.

As indicated in Table 4, compared to the EAR for pregnant women ages 19–30, the majority of all women were likely deficient (greater than 50% <EAR) in all micronutrients except three: niacin, phosphorus, and selenium. Using the less stringent nutrient requirements for non-pregnant females aged 19–30, the majority still had likely inadequate intake for 10 (vitamin A, D, E, C, B₆, total folate, B₁₂, calcium, magnesium, and zinc) of the 16 micronutrients with established EARs. The majority of all women are likely adequate on selenium (58% > RDA), yet no mother exceeded the potentially toxic upper tolerable limit of 400mcg. Conclusions about nutrient intakes between EAR and RDA cannot be easily made; however, niacin and phosphorus intake is likely suboptimal for many women in this study. Of the nutrients presented here with established EARs, only vitamin D registered a significant difference in the proportion of women likely inadequate among maternal groups, such that fewer mothers of children with FASD were likely to be inadequate ($p=.002$). Vitamin B₁₂ and magnesium approached significance with a similar pattern where fewer mothers of children with FASD were likely inadequate. Regardless of child diagnostic category, all mothers were deficient on nearly all micronutrients compared to the dietary reference intake (DRI).

Data were collected to determine the similarity of eating habits at the time of the interview as compared to that during the pregnancy of the index child. Significantly more mothers of children with FASD reported consuming less food during pregnancy (33%) as compared to at the time of the interview ($Z=1.98$, $p=.044$) and 19% ate the same during pregnancy. Twelve percent (12.3%) of mothers with children with FASD reported multivitamin use during pregnancy compared to 18.4% of control mothers, which is not significantly different. The majority (>87%) of all mothers breastfed their child with a mean duration of 18.2 months, and there was no difference at all between groups.

In Table 5 specific nutrients are correlated with selected child characteristics. Ten and eight of the nutrients are significantly, negatively correlated with child BMI and OFC. Maternal BMI are positively correlated with child OFC, BMI, palpebral fissure length (PFL), verbal IQ, and non-verbal IQ, while negatively correlated with total dysmorphology score. Overall, the greater the mother's BMI, the better the outcome for all child traits, and the less maternal intake of essential nutrients, the higher the child's BMI. Regarding binge drinking, only two nutrients were significantly correlated with any of the bingeing. Calcium intake is

significantly lower in mothers who binge drink ($p<.05$) while EPA intake is higher among those who binge drink.

4. DISCUSSION

These data indicate that the majority of ZA women in this sample consumed inadequate amounts of nearly all micronutrients. No clear deficiency disease is present in the sample, but the overall and specific micronutrient deficiencies found in this sample are important. DRI for micronutrients is higher for pregnant women, and the vast majority of the women in this study did not even meet the DRI for most micronutrients for normal (non-pregnant) females, aged 19–30. While individual nutrient deficiencies are important to overall health, deficiencies rarely appear in isolation, and inter-nutrient interactions often necessitate adequate levels of all nutrients to maintain vigor of body.

Dietary staples among this population include meat and vegetable stews (often with potatoes, onions, green beans, cabbage and/or chicken, beef or lamb), eggs, tea with full cream milk and sugar, instant coffee, porridge (often maize), white rice, and white bread with margarine. Many women reported consuming one main meal and consuming coffee and/or tea with slices of white bread with margarine throughout the day. Few fruits or commercially-prepared foods were reported. Many women in this community, particularly those of low SES, would benefit from increased access to healthy foods and a vitamin/mineral supplement to meet their nutrient needs, especially during pregnancy.

Even though mothers of children with FASD consumed more total protein, vitamin E, C, B₆, magnesium, phosphorus, EPA, DHA, and DPA than did mothers of controls, this difference may not have been biologically significant since all mothers were found to be deficient. Consuming more micronutrients could have been advantageous to fetal development, as many studies have shown that slight differences in diets of pregnant animals can lead to altered morphology, physiology, and performance in offspring [28–30]. However, excessive alcohol consumption likely nullified the beneficial effects of additional, albeit still deficient, nutrient intake in the mothers of children with FASD. This indicates that despite an increase in total food consumption in mothers of children with FASD, there was no corresponding increase in diet quality.

The mean drinking data in this sample (Table 2) clearly show a dose-response effect for alcohol across groups and the child outcome data also follow a dose-response pattern. For example, women with significantly lower weight who drank significantly more than mothers of controls were more likely to have a child with FASD regardless of whether they had a statistically significant higher average intake of a dozen or more essential nutrients than mothers of controls. In spite of the higher intake of vitamins D, C, B₁₂, thiamin, pantothenic acid, phosphorous, magnesium, selenium, potassium, and 3 essential fatty acids (EPA, DPA, and DHA) than controls, the overall nutrient deficiency status did not protect or enhance fetal development. Furthermore, child outcomes were poorer for most variables for children with FASD and alcohol-exposed children, consistently exhibiting the poorest outcomes in an alcohol exposure dose-response pattern: height, weight, head circumference, total dysmorphology, verbal IQ, and behavioral problems. Child BMI and non-verbal IQ are the

only partial exceptions, as the alcohol-exposed controls were slightly better than unexposed controls.

The mean dietary intakes of nutrients that differed among diagnostic groups are necessary for specific cellular and metabolic pathways that are vital to fetal growth and development. Vitamin D aids the gastrointestinal absorption of other nutrients, including calcium, phosphate, magnesium, iron, and zinc. While some foods contain vitamin D, the majority of vitamin D is synthesized in the skin after ultraviolet light (sun) exposure. Antioxidants, such as vitamin E and C, help protect cells by acting as free radical scavengers. Vitamin C keeps free radicals from reaching the cell's membrane while vitamin E attempts to stabilize free radicals. Other free radical scavengers and antioxidant enzymes are dependent on essential nutrients such as magnesium, riboflavin, and niacin for activation. The vitamin B-complex is essential for cellular function, formation of neurotransmitters, and metabolism of glucose, lipids, proteins, and alcohol. Phosphate and magnesium ions are essential components of nucleic acids. Hundreds of enzymes, including nucleotides required to synthesize DNA and RNA, require magnesium as a catalytic agent. Phosphate is also a key structural element of RNA and DNA. Selenium is an essential trace element and a cofactor for antioxidant enzymes and thyroid hormones. Potassium assists in maintaining osmotic balance and cellular membrane polarization as well as being involved in protein synthesis and carbohydrate metabolism. DHA is particularly important in cognitive development [31,32]. EPA also shows promise as a bioactive nutrient to promote brain development and function [33], and its mechanisms on developmental processes mirror those of DHA [34,35].

The nutritional requirements of the fetus represent a cost to the mother and nutrients available to the fetus are dependent on the mother's intake, her metabolism, her partitioning of nutrients among maternal stores and circulation, and the placental transport mechanism. Undernourished mothers, like those in this sample, may be limited in their ability to appropriately support the fetus. Despite the mothers of children with FASD consuming higher quantities of micronutrients, alcohol has been shown to affect the absorption, distribution, and excretion of micronutrients. Alcohol can disrupt the fetal supply of nutrients through multiple mechanisms including: 1) quality and quantity of intake can decrease [36]; 2) gastrointestinal changes may lead to abnormal digestion and malabsorption of nutrients [37]; 3) decreased renal function/reabsorption and increased urine excretion of key micronutrients [37,38]; 4) alterations in the composition and function of gut microbiome [39]; and 5) altered placental transport and placental metabolism of nutrients [40,41]. Furthermore, pathways which metabolize ethanol are dependent, at least partially, on nutritional factors [1]. Independent of the shortage of micronutrients, which may have aided or protected fetal development, it is plausible that the alcohol further reduced the available nutrients for the fetus.

Correlation analyses indicate that maternal intake of calcium, iron, and zinc is positively associated with child verbal and non-verbal IQ at age seven. This is consistent with other studies which indicate that iron [3,43] and zinc [44] are essential for long-term cognitive development. Child OFC, PFL, and dysmorphology scores are significantly, negatively associated with many of the maternal nutrients. Maternal BMI and maternal weight have been positively associated with better child outcomes (less dysmorphology, high verbal and

non-verbal IQ, and fewer problem behaviors) in previous studies in this ZA population [11,13–15]. Women with higher weight and BMI have greater amounts adipose tissue which helps distribute the alcohol, allowing less alcohol to across the placenta. Like nutrition, other maternal variables, such as BMI and length of drinking career, influence the complex maternal/fetal interactions [45]. These associations lend credence to the idea that maternal/fetus nutrient exchange is a complex interaction between the mother, placenta, and fetus, which in this sample we found that marginally higher maternal intake does not necessarily equate to better child outcomes [46,47].

Many studies associate breastfeeding with improved child cognition [48]. A higher concentration of omega-3 fatty acids, specifically DHA, in breastmilk has been identified as one of the nutrients responsible for the positive association between breastfeeding and development [49]. In this sample most women (>87%) initiated breastfeeding and maintained breastfeeding for an average of 18 months. Given that almost half (43%) of the women in this sample drank alcohol while breastfeeding and the many nutritional deficits in this sample, newborns may have been at a continued, double postpartum nutrient disadvantage due to inadequate intake of nutrients through breastmilk and further exposure to the teratogenic effect of alcohol for the critical first 18 months of life. Proper nutrition in the first 2 years of life is essential to future cognitive development [50,51], and nutritional deficiencies during brain development can have irreversible changes in structure and function [48]. Independent of alcohol exposure, in utero malnutrition, followed by poor postnatal nutrition, can perpetuate the effect of malnutrition, which can cause severely stunted growth [52] and negatively influence reasoning, visuospatial functions, IQ, language development, attention, learning, and academic achievement [48].

The previous study in this community with a completely different sample of mothers and children produced comparable dietary intake and maternal risk patterns for child outcomes [18]. In both samples, the majority of all women were below the EAR on the same 12 of 16 nutrients with established EARs. In the previous sample, however, the mothers of children with FASD consumed, on average, smaller quantities of these vital nutrients and a greater proportion of these mothers were likely inadequate of most nutrients than controls. In the current sample, mothers of children with FASD consumed slightly greater quantities of many nutrients; however, only one micronutrient had a statistically significant difference between maternal groups in the proportion of women who were likely inadequate. Despite the higher dietary intake averages for the mothers of children with FASD, alcohol likely diminishes any beneficial effects of additional micronutrients.

4.1 Limitations

A major limitation of this study is that dietary intake information was collected for a 24-hour period seven years after the index child was born. Although the questions attempted to link the data to the pregnancy, changes in diet and recall could negatively impact the study. Because of the individual variation in nutrient requirements, food preparation, and other uncontrolled influences, determining adequacy is difficult; however, nutrient intake evaluation followed IOM recommendations [27]. Given this small and unique sample of mother/child dyads, it is difficult to generalize these findings to other populations [53]. But

the overall findings indicate that the majority of women in this community with an extremely high rate of FASD are likely deficient on many micronutrients are insightful. A second limitation is that the environment effect (stimulation or stultifying) on child outcomes cannot be fully understood in these types of analyses. While individual-level environmental factors have been associated with having a child with FASD [45], changing these conditions in the short-term is difficult. But over time improvement in social conditions may result in better birth and child development outcomes. A third limitation is the lack of blood samples which could have been used to validate the nutrient estimations obtained through the 24-hour dietary recall, as some bias may have been introduced by using an American database to estimate the nutritional composition of ZA foods. Blood analysis allows for more definitive conclusions regarding maternal nutrient status. But, given the high proportion of mothers who were below EAR and the significant magnitude of the deficiencies, it is likely that the mothers are truly deficient. Fourth, dietary intake studies cannot tell us about genetically or epigenetically determined patterns of maternal metabolism of these nutrients. Further we do not know how the microbiome of the maternal digestive system affects availability of nutrients to the fetus or whether the gut flora itself exacerbates the pathophysiology of FASD due to endogenous ethanol synthesis [54]. Other methods employed in other studies are needed to get beyond average nutritional analysis and for determining individual variation from one mother to the next and one child to the next, especially with the presence of alcohol in the equation.

5. CONCLUSION

These results support previous studies which indicate that people who consume large quantities of alcohol may be at an additional nutritional disadvantage because chronic alcohol use can cause malabsorption or altered metabolism of nutrients. These results reinforce our understanding that maternal dietary intake during pregnancy is an important co-factor of risk for FASD, and suggest that nutritional status of the mother may further exacerbate the effect of alcohol on child outcomes. Our results provide insight into possible mechanisms of FASD pathophysiology that warrant further study. The specific biochemical defects that occur due to the combination of overconsumption of alcohol and undernutrition and the biological parameters in the mother, such as epigenetics and the microbiome, that modulate long term health outcomes of the offspring are poorly understood. Future studies to address these gaps in knowledge will be essential for the development of individualized prevention and treatment strategies.

Acknowledgments

Partial funding was provided by the NIAAA (U01 AA11685) and the Foundation for Alcohol Related Research (FARR). We thank the women who provided the information for this study. Protocols and consent forms used were approved by the University of New Mexico (Medical School HRRC 96-209 and 00-422, and Main Campus IRB 9625), the Ethics Committee of the University of Cape Town, and a local, single site assurance committee.

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Highlights

- Dietary intake among South Africa women is compared to recommended intake values.
- Nearly all mothers were significantly below reference intakes for most nutrients.
- Alcohol overpowered slight advantages of higher intake in mothers of FASD group.
- Nutrient inadequacies with prenatal alcohol exposure increase the risk for FASD.

Table 1

Demographic and Growth Parameters, Educational Testing and Behavioral Measures for the Sample of South African Children with FASD and Randomly-selected Controls in the Western Cape Province (WCP) of South Africa

	Children with FASD (n=57)	Exposed Controls (n=42)	Unexposed Controls (n=106)	p-value
Sex (% Males)	56.1	45.2	51.9	.562
Age (months) – Mean (SD)	92.6 (7.9)	87.4 (5.1)	87.2 (5.9)	<.001 ^{a,b}
Height (centile) – Mean (SD)	4.9 (6.2)	21.2 (26.6)	28.6 (23.7)	<.001 ^{a,b}
Weight (centile) – Mean (SD)	3.4 (2.4)	20.2 (25.1)	29.3 (24.9)	<.001 ^{a,b}
Occipital Circumference (centile) – Mean (SD)	3.8 (4.2)	22.0 (24.2)	29.3 (26.3)	<.001 ^{a,b}
BMI (centile) – Mean (SD)	15.9 (15.7)	34.3 (25.5)	29.3 (23.9)	<.001 ^{a,b}
Dysmorphology Score – Mean (SD)	18.2 (3.4)	11.0 (5.0)	8.6 (4.4)	<.001 ^{a,b,c}
Educational Testing and Behavior				
Verbal IQ – Mean (SD) ¹	75.4 (11.5)	86.2 (15.3)	86.5 (11.4)	<.001 ^{a,b}
Non-verbal IQ – Mean (SD) ²	77.9 (6.3)	87.1 (10.3)	85.4 (9.1)	<.001 ^{a,b}
Behavior (PBCL36) – Mean (SD) ³	12.1 (8.3)	6.5 (7.9)	5.8 (7.6)	<.001 ^{a,b}

Significant Dunnett C comparison post-hoc significant (<.05) difference between:

^a mothers of children with FASD & mothers of exposed control children;

^b mothers of children with FASD & unexposed control children;

^c mothers of children of exposed controls & unexposed controls.

Table 2

Maternal Physical, Demographic, Socioeconomic, Childbearing and Alcohol Use Variables for Mothers of Children with FASD and Randomly-selected Controls in the WCP

	Children with FASD (n=57)	Exposed Controls (n=42)	Unexposed Controls (n=106)	P-value
Demographic and Socioeconomic Variables				
Age on day of interview (yrs) - Mean (SD)	36.1 (7.1)	33.1 (5.8)	34.2 (5.9)	.054
Height (cm) - Mean (SD)	154.8 (5.9)	155.4 (10.6)	157.6 (6.0)	.037 ^b
Weight (kg) - Mean (SD)	54.5 (14.7)	61.9 (13.1)	68.8 (18.8)	<.001 ^{a,b,c}
Head circumference (cm) - Mean (SD)	54.8 (1.9)	54.9 (2.0)	54.8 (1.7)	.986
Body Mass Index (BMI) - Mean (SD)	22.7 (5.6)	25.2 (5.2)	27.7 (7.5)	<.001 ^b
Residence during index pregnancy (%)				
Rural	71.4	50.0	25.5	
Urban	28.6	50.0	74.5	<.001
Educational attainment at interview (yrs) - Mean (SD)	5.0 (2.8)	6.9 (3.4)	8.2 (2.8)	<.001 ^{a,b}
Current income (Rands per week) - Mean (SD)	421.5 (283.8)	698.9 (758.4)	772.8 (780.0)	.008 ^b
Childbearing Variables				
Gravidity - Mean (SD)	3.5 (1.6)	3.0 (1.5)	2.9 (1.3)	.027 ^b
Parity - Mean (SD)	3.1 (1.2)	2.8 (1.3)	2.6 (1.1)	.002
Miscarriages - Mean (SD)	.4 (.7)	.2 (.4)	.2 (.4)	.129
Stillborn - Mean (SD)	.1 (.3)	.0 (.2)	.0 (.1)	.080
Age at Birth of the Index Child - Mean (SD)	27.6 (6.7)	24.5 (5.4)	26.0 (5.8)	.049 ^c
Marital status during pregnancy with index child (%)				
Married	19.3	16.7	46.2	
Unmarried, living with partner	17.5	21.4	29.2	
Unmarried, living with parents	49.1	42.9	13.2	
Separated/Divorced/Widowed/Single	14.0	19.0	11.3	<.001
Alcohol Consumption Variable				
Current Drinking (at time of interview)				
Current drinkers (drank within last year) (%)	100	100	43.4	<.001
Current number of drinks per week - Mean (SD)	5.1 (8.4)	4.9 (7.3)	2.2 (5.5)	.385
Binged (3+) in week preceding interview (%)	28.1	26.2	1.0	<.001
During Pregnancy				
Reported alcohol consumption during pregnancy (%)	91.2	100	0.0	<.001
# of drinks per week in 1 st trimester - Mean (SD)	11.8 (12.8)	5.4 (6.9)	.0 (.0)	<.001 ^{a,b,c}
Drinks per drinking day in 1 st trimester - Mean (SD)	5.0 (3.7)	3.2 (3.3)	.0 (.0)	<.001 ^{a,b,c}
# of drinks per week in 2 nd trimester - Mean (SD)	10.4 (13.0)	4.0 (6.7)	.0 (.0)	<.001 ^{a,b,c}
Drinks per drinking day in 2 nd trimester - Mean (SD)	4.3 (3.9)	2.3 (3.2)	.0 (.0)	<.001 ^{a,b,c}

	Children with FASD (n=57)	Exposed Controls (n=42)	Unexposed Controls (n=106)	P-value
# of drinks per week in 3 rd trimester – Mean (SD)	9.3 (13.2)	3.6 (6.6)	.0 (.0)	<.001 ^{a,b,c}
Drinks per drinking day in 3 rd trimester – Mean (SD)	3.8 (4.0)	2.0 (3.1)	.0 (.0)	<.001 ^{a,b,c}

Significant Dunnett C comparison post-hoc significant (<.05) difference between:

^a mothers of children with FASD & mothers of exposed control children;

^b mothers of children with FASD & unexposed control children;

^c mothers of children of exposed controls & unexposed controls.

Table 3

Comparison of Nutrient Intake by Estimated Average Requirement (EAR) and Adequate Intake (AI) among Mothers of Children with an FASD and Exposed and Unexposed Controls, WCP, South Africa

	EAR/AI	All women (n=205)		p- value ¹	Mothers of Children with FASD (n=57)		Mothers of Exposed Controls (n=42)		Mothers of Unexposed Controls (n=106)		p- value ²
		Mean	(SD)		Mean	(SD)	Mean	(SD)	Mean	(SD)	
Total Grams	NA	1423	(514)	--	1472	(665)	1499	(576)	1367	(377)	.267
Energy (kcal)	NA	1263	(526)	--	1373	(661)	1303	(491)	1187	(445)	.084
Total fat (g)	NA	44.0	(30.6)	--	47.5	(34.4)	43.8	(23.4)	42.2	(31.0)	.576
Total carbohydrate (g)	135++	164.2	(60.7)	<.001	176.2	(77.0)	166.3	(58.4)	156.8	(50.4)	.146
Total protein (g)	50++	49.7	(25.3)	.847	56.3	(31.9)	48.9	(24.5)	46.4	(20.8)	.055
Dietary fiber (g)	28++	11.8	(6.4)	<.001	12.2	(5.8)	12.1	(8.0)	11.4	(5.9)	.670
Cholesterol (mg)	300+++	174.9	(139.2)	<.001	191.9	(148.5)	178.9	(147.5)	164.2	(130.9)	.473
Vitamin A (retinol equiv)(mcg)	550 ⁺	389.6	(439.1)	<.001	429.3	(486.6)	383.4	(509.0)	370.7	(382.1)	
Vitamin D (mcg)	10 ⁺	3.8	(7.0)	<.001	6.5	(10.9)	2.8	(5.1)	2.8	(4.1)	.003 ^a
Vitamin E (mg)	12 ⁺	3.3	(2.9)	<.001	4.0	(3.2)	3.0	(3.0)	3.0	(2.6)	.097
Vitamin K (mcg)	90++	43.7	(42.6)	<.001	44.7	(34.3)	39.2	(21.1)	45.0	(52.2)	.743
Vitamin C (mg)	70 ⁺	36.6	(49.6)	<.001	52.8	(69.9)	27.3	(31.2)	31.5	(40.0)	.012 ^b
Thiamin (mg)	1.2 ⁺	1.1	(.5)	.042	1.3	(.6)	1.2	(.5)	1.1	(.4)	.033 ^a
Riboflavin (mg)	1.2 ⁺	1.2	(.5)	.595	1.2	(.6)	1.2	(.6)	1.1	(.4)	.580
Niacin (mg)	14 ⁺	15.7	(8.0)	.002	17.7	(9.8)	15.8	(8.3)	14.6	(6.5)	.055
Pantothenic Acid (mg)	6 ⁺⁺	4.0	(1.9)	<.001	4.4	(2.1)	4.3	(2.6)	3.6	(1.3)	.033
Vitamin B ₆ (mg)	1.6 ⁺	1.0	(.6)	<.001	1.2	(.7)	1.0	(.7)	.9	(.5)	.119
Total Folate (mcg)	520 ⁺	237.2	(116.8)	<.001	244.8	(100.3)	246.4	(129.1)	229.6	(120.5)	.624
Vitamin B ₁₂ (mcg)	2.2 ⁺	3.6	(8.5)	.020	6.1	(14.9)	2.5	(3.6)	2.7	(3.6)	.032
Calcium (mg)	800 ⁺	433.5	(253.4)	<.001	413.1	(247.8)	460.7	(370.4)	433.6	(194.7)	.655
Phosphorus (mg)	580 ⁺	639.5	(322.2)	.009	742.8	(423.4)	619.2	(290.9)	592.0	(254.5)	.015 ^a

	All women (n=205)	P- value ¹	Mothers of Children with FASD (n=57)		Mothers of Exposed Controls (n=42)		Mothers of Unexposed Controls (n=106)		P- value ²
			EAR/AI	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Magnesium (mg)	290 ⁺		148.9 (72.3)	<.001	169.7 (102.2)	148.9 (68.4)	137.7 (48.9)	.026	
Iron (mg)	22 ⁺		8.5 (3.9)	<.001	8.6 (3.6)	9.0 (5.5)	8.2 (3.3)	.562	
Zinc (mg)	9.5 ⁺		5.9 (3.3)	<.001	5.9 (3.5)	6.3 (4.3)	5.8 (2.8)	.759	
Selenium (mcg)	49 ⁺		75.7 (45.2)	<.001	93.4 (58.2)	65.4 (27.4)	70.2 (40.4)	.002 ^{a,b}	
Sodium (mg)	1500 ⁺⁺		2015.1 (871.1)	<.001	2311 (1066)	1954 (790)	1879 (745)	.009 ^a	
Potassium (mg)	4700 ⁺⁺		1540.3 (701.9)	<.001	1731 (937)	1571 (755)	1424 (480)	.027	
Choline (mg)	450 ⁺⁺		219.0 (122.7)	<.001	250.9 (135.0)	219.1 (126.3)	201.8 (111.5)	.051	
Omega-3 fatty acids (g)	1.4		1.352 (1.696)	.689	1.773 (2.003)	1.209 (1.127)	1.184 (1.746)	.088	
Eicosapentanoic acid (EPA) (g)	NA		.094 (.260)	--	.215 (.429)	.043 (.114)	.049 (.129)	<.001 ^{a,b}	
Docosapentanoic acid (DPA) (g)	NA		.036 (.078)	--	.064 (.107)	.029 (.089)	.023 (.045)	.006 ^a	
Docosahexaenoic acid (DHA) (g)	NA		.149 (.417)	--	.316 (.107)	.087 (.260)	.084 (.195)	.002 ^a	

¹ One sample t-test comparing the mean for all women to EAR/AI;

² ANOVA comparing mothers of children with FASD, alcohol-exposed and unexposed controls.

⁺ Estimated Average Requirement (EAR) for pregnant women, aged 19–30, used for: carbohydrate, protein, vitamin A, C, D, E, thiamin, riboflavin, niacin, vitamin B₆, folate, vitamin B₁₂, calcium, phosphorus, magnesium, iron, zinc, and selenium.

⁺⁺ Adequate Intake (AI) for pregnant women, aged 19–30, used for dietary fiber, vitamin K, pantothenic acid, sodium, potassium, choline, and omega-3 fatty acids.

⁺⁺⁺ IOM recommends intake to be “as Low As Possible while consuming a nutritionally adequate diet”: <300mg recommended by USDA.

[#] Percentage less than EAR is not reported for nutrients where the Institute of Medicine deemed there is insufficient evidence to establish an EAR.

Significant post-hoc difference (p<.05) between:

^a mothers of children with FASD and unexposed controls;

^b mothers of children with FASD & exposed controls

Table 4

Comparison of Nutrient Intake compared to Dietary Reference Intake (DRI) among Mothers of Children with an FASD, and Alcohol-Exposed and Unexposed Controls, WCP, South Africa

	EAR ⁺	All women ^I (n=205) % less than EAR	Mothers of Children with FASD (n=57) % less than EAR	Mothers of Exposed Controls (n=57) % less than EAR	Mothers of Unexposed Controls (n=106) % less than EAR	p- value
Vitamin A (retinol equiv)(mcg)	550	68.3	63.2	73.8	68.9	.522
Vitamin D (mcg)	10	91.7	80.7	95.2	96.2	.002
Vitamin E (mg)	12	97.6	94.7	97.6	99.1	.234
Vitamin C (mg)	70	83.4	75.4	85.7	86.8	.161
Thiamin (mg)	1.2	58.5	54.4	54.8	62.3	.533
Riboflavin (mg)	1.2	59.5	54.4	61.9	61.3	.649
Niacin (mg)	14	48.3	40.4	47.6	52.8	.210
Vitamin B ₆ (mg)	1.6	88.8	86.0	83.3	92.5	.208
Total Folate (mcg)	520	96.6	96.5	97.6	96.2	.914
Vitamin B ₁₂ (mcg)	2.2	56.1	43.9	66.7	58.5	.060
Calcium (mg)	800	92.7	94.7	85.7	94.3	.150
Phosphorus (mg)	580	48.8	40.4	45.2	54.7	.293
Magnesium (mg)	290	97.1	93.0	97.6	99.1	.088
Iron (mg)	22	99.5	100	97.6	100	.142
Zinc (mg)	9.5	88.8	86.0	95.2	87.7	.312
Selenium (mcg)	49	28.8	24.6	31.0	30.2	.655

^I All women category is excluded from the chi-square comparisons.

⁺ Estimated Average Requirement (EAR) for pregnant women, aged 19-30, used for: carbohydrate, protein, vitamin A, C, D, E, thiamin, riboflavin, niacin, vitamin B₆, folate, vitamin B₁₂, calcium, phosphorus, magnesium, iron, zinc, and selenium.

Table 5
Bi-variate Correlations of Nutrient Intake Deficiencies with Selected Child Characteristics

	Head Circumference (OFC)	Child BMI	Palpebral fissure length (PFL)	Dysmorphology Score ¹	Verbal IQ (TROG)	Non-verbal IQ (Raven)	Behavior (PBCL-36) ²	Binged 3 during pregnancy	Binged 5 during pregnancy
Total carbohydrate	-.147*	-.206**	-.176*	.138*	.013	-.054	.004	-.006	.022
Total protein	-.182**	-.162*	-.119	.110	.007	-.046	.062	.037	.111
Vitamin E	-.064	-.065	-.061	.024	.152*	.114	-.083	-.018	.053
Thiamin	-.107	-.186**	-.133	.117	.037	-.021	.092	.067	.024
Niacin	-.140*	-.168*	-.107	.076	.038	-.022	.052	.059	.121
Total folate	.018	.012	-.017	-.021	.110	.154*	-.036	-.038	-.025
Calcium	-.003	-.048	.030	-.120	.237**	.139*	-.127	-.185**	-.112
Phosphorus	-.167*	-.152*	-.130	.115	.020	-.019	.041	-.018	.059
Magnesium	-.169*	-.185**	-.130	.144*	.029	-.061	.018	.043	.105
Iron	-.044	-.054	-.009	-.052	.205**	.142*	-.020	-.073	-.004
Zinc	-.065	-.029	.054	-.091	.237**	.156*	.012	-.065	-.021
Selenium	-.131	-.205**	-.127	.127	-.066	-.081	.085	.057	.100
Sodium	-.142*	-.246**	-.167*	.131	-.048	-.062	.141*	.066	.075
Potassium	-.178*	-.175*	-.131	.133	.066	-.023	.009	.028	.099
EPA	-.102	-.146*	-.145*	.162*	-.084	-.113	.079	.137*	.137
DPA	-.121	-.095	-.137*	.176*	-.078	-.102	.099	.115	.137
DHA	-.089	-.128	-.131	.154*	-.039	-.082	.052	.107	.123
Choline	-.186**	-.109	-.148*	-.125	-.074	-.064	-.029	.011	.102
Maternal BMI	.289**	.311**	.298**	-.374**	.229**	.194**	-.119	-.214**	-.146*

* p .05;

** p .01

¹ High scores meaning more dysmorphology

High scores meaning more gunning behaviors

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