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Omega-6 fatty acids and greater likelihood of suicide risk and major depression in early pregnancy

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ABSTRACT

Objective: To estimate the prevalence of suicide risk (SR) and major depressive episodes (MDEs) in early pregnancy, as well as the relationship of serum fatty acid status to these outcomes.
Methods: Cross-sectional analyses were performed on data from 234 pregnant women enrolled in a prospective cohort study in Rio de Janeiro, Brazil. SR and MDE were defined according to the Mini International Neuropsychiatric Interview. Fatty acid compositions were determined for serum samples obtained between the 6th and 13th gestational week. Fatty acid data were expressed as the percent of total fatty acids, converted to Z scores and then entered as continuous variables in logistic regression models.
Results: The prevalence of SR was 19.6% and that of MDE was 17.0%. In the adjusted logistic regressions, a higher likelihood of SR was observed among women with higher arachidonic acid levels [AA (20:4, n-6): OR=1.45, 95%CI 1.02–2.07] and adrenic acid levels [AdA (22:4, n-6): OR=1.43, 95%CI 1.01–2.04]. A higher likelihood of MDE was also observed among women with higher AA levels [OR=1.47, 95%CI 1.03–2.10] and AdA levels [OR=1.59, 95%CI 1.09–2.32].
Conclusion: Higher serum levels of AA and AdA were associated with a greater likelihood of SR and MDE among pregnant Brazilian women.

Significant outcomes

- Our study determined serum fatty acid composition during early pregnancy and identified suicide risk (SR) and major depressive episodes (MDE) based on a diagnostic psychiatric interview.
- In multiple adjusted regression models, each increase of one standard deviation in serum arachidonic acid (AA) and adrenic acid (AdA) levels—two omega-6 fatty acids—was associated with a greater likelihood of SR and MDE in early pregnancy, independent of confounding variables.
- Our findings suggest that higher serum AA and AdA levels may be a consequence of a Western dietary pattern, caracterized by higher consumption of omega-6 and lower consumption of omega-3 fatty acids.

Limitations

- The analysis was cross-sectional, which limits the ability to establish whether the association between exposure and outcome is a true cause-effect relationship.
- Our results are derived from Brazilian pregnant women of low socioeconomic status. Further studies are needed to confirm our findings in other population groups.

1. Introduction

Pregnancy creates substantial hormonal and physiological changes, is often followed by stressful social transitions and is a vulnerable time for the onset of mental disorders (Christian, 2012). Although post-partum depression has been extensively evaluated, less is known about the occurrence and biological determinants of suicide risk (SR) and major depression episodes (MDEs) in early pregnancy. Deficiencies or excesses in neuro-active nutrients that are selectively concentrated in neural tissues, specifically highly unsaturated omega-3 (n-3 HUFA) and omega-6 (n-6 HUFA) fatty acids, may contribute to susceptibility to these disorders (Hibbeln

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and Davis, 2009). Neither n-3 nor n-6 fats cannot be synthesized by humans, so they must be obtained from the diet. Fish is a rich source of both n-3 and n-6 HUFAs, and lower intakes have been associated with increased risk for depressive symptoms and suicidal thinking in cross-national and cohort-based studies; while the majority of blood-based studies indicate that n-3 HUFAs are protective, n-6 HUFAs have been associated with increased risk [For review see (Hibbeln, 2009; Milte et al., 2009)]. Meta-analyses of randomized controlled trials have indicated that n-3 HUFA supplementation has an efficacy similar to that of fish oils and pharmaceutical antidepressants in reducing significant depressive symptoms (Sublette et al., 2011; Lin et al., 2010).

The putative role of n-3 and n-6 HUFAs in depressive symptoms and SR is less clear. Selective transportation of HUFAs across the placenta not only biomagnifies concentrations to the fetus but may also lead to maternal depletion when dietary intake is insufficient. In an epidemiological investigation, Golding et al., (2009) found that mothers with low seafood intake during pregnancy were at increased risk for depression. Randomized controlled intervention trials during the perinatal period have shown promise but have been difficult to adequately design and conduct (Jans et al., 2010). SR during pregnancy has become a subject of increasing interest, but much less is known about its occurrence and the role of fatty acids. Lower levels of n-3 HUFA docosahexaenoic acid (DHA; 22:6, n-3) were associated with an increase in suicide deaths among 1600 active duty US Military personnel (Lewis et al., 2011), and one intervention trial with n-3 HUFAs reported a 45% reduction in suicidal ideation (Hallahan et al., 2007).

Thus, in the present study, we sought to evaluate possible relationships between maternal serum n-3 and n-6 HUFA status and SR and MDE in early pregnancy. Our primary hypothesis was that lower n-3 HUFAs, in particular DHA, would represent a greater risk for suicidality and major depression. To our knowledge, this is the first epidemiological study on mood disorders among Brazilian pregnant women that investigates blood fatty acid levels. Evaluation of these issues in a Brazilian population, with biological samples, adds diversity to the body of data on HUFA status in pregnancy and potential psychiatric risks.

2. Methods

2.1. Study protocol

2.1.1. Design

The current investigation originated from a broader study with a prospective cohort design that was performed in the city of Rio de Janeiro, Brazil. Enrollment of pregnant women in the cohort was open for 23 months (November 2009–October 2011). Baseline assessment was performed between the 6th and the 13th week of gestation. At that time, blood collection and a psychiatric interview were conducted, followed by a general questionnaire (socioeconomic data, obstetric history, lifestyle, scales) and anthropometric assessment (body weight and stature). All interviews were conducted during appointment days at a pre-natal care center of the Brazilian Unified Health System.

The eligibility criteria were defined as follows: being between the 6th and 13th week of gestation; being between 20 and 40 years of age; being free from any chronic diseases such as hypertension and diabetes; carrying a single fetus not presenting twin pregnancy, and residing in the study catchment area. During the recruitment phase, a continuous on-site researcher interviewed all women who accessed pre-natal care for the first time. Women who met the eligibility criteria were invited to join the study. Ninety-three percent of eligible women agreed to participate and were scheduled for an appointment for blood collection and clinical assessment.

2.2. Psychiatric assessment

Psychiatric interviews were conducted using the Mini International Neuropsychiatric Interview (MINI; version 5.0.0) (Sheehan et al., 1998), an instrument with a standard model of a brief (15–30 min) structured interview for the evaluation of the presence of Axis I psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (American Psychiatric Association, 2000). This instrument is divided into modules (A–P), which each contain questions that represent different psychiatric disorders. The patients must answer yes or no to each of the questions. The interviews were performed by medical doctors and graduate students in mental health who were trained for this purpose.

SR was assessed by means the 'suicidality' level obtained from the MINI interview. In this module, six questions were asked, and positive answers received a unique score, as follows: "In the past month did you: (Christian, 2012) think that you would be better off dead or wish you were dead? (Score=1); (Hibbeln and Davis, 2009) want to harm yourself or to hurt or to injure yourself? (Score=2); (Hibbeln, 2009) think about suicide? (Score=6); (Milte et al., 2009) have a suicide plan? (Score=10); (Sublette et al., 2011) attempt suicide? (Score=10); (Lin et al., 2010) during your past, did you ever make a suicide attempt? (Score=4)." In this instrument, a positive answer to at least one of these features is considered representative of SR. This variable was entered as binary (SR=yes/no) in the logistic regression. The MDE module provided the patient's current status (yes or no) and was entered as binary (MDE=yes/no) in the logistic regression. For the present investigation, both SR and MDE were considered dependent variables, and a theoretical model was built for each outcome.

2.3. Independent variables

To build the theoretical model for SR and MDE, the following independent variables were included in the analyses: socioeconomic status, indicated by monthly per capita family income (in tertiles of American dollars); socio-demographic bracket, indicated by age (20–29, 30–40 years), marital status (married or stable relationship, single), self-reported skin color (white, non-white), education (≤8, ≥9 years), work status (yes, no); lifestyle, indicated by smoking habit (yes, no), current alcohol consumption (yes, no), hours of nighttime sleep (<8, ≥8 h); obstetric history, indicated by parity (0, 1, ≥2), previous history of spontaneous abortion (yes, no), desire to be pregnant (yes, no); home crowding, defined as number of people per room (<2, ≥2); and reported family history of depression (first-degree relative) (yes, no), reported family history of suicide (first-degree relative) (yes, no). Additionally, the following confounding factors were also considered: number of close friends (0–1, ≥2) and number of close relatives (0–1, ≥2).

Nutritional status was included in the theoretical model defined by pre-pregnancy body mass index (BMI [weight (kg)/stature (m^2)]) obtained at baseline (between the 6th and 13th week). The cut-off points proposed by the World Health Organization (Physical status, 1995), and recently endorsed by the Institute of Medicine, were considered for the classification of the women's initial nutritional status (Weight Gain During Pregnancy, 2009). The women were weighed with a digital scale (Filizzola Ltd., São Paulo, Brazil). Stature was measured in duplicate with a Seca Portable Stadiometer (Seca Ltd., Hamburg, Germany). All anthropometric measurements were standardized and taken by trained interviewers (Lohman et al., 1998).

2.4. Sample analysis

Blood samples (5 ml) from each woman were collected into vacutainer tubes with separator gel by a health clinic professional during the 1st clinical visit, when the women had completed ≤13 weeks of pregnancy. The women were advised to fast for 12 hours. Serum and plasma were separated after centrifugation (5000 rpm) for 5 min and stored at −80 °C for later measurements. To determine the blood fatty acid composition, serum samples were shipped on dry ice to the Department of Nutritional Neurosciences, Laboratory of Membrane Biochemistry and Biophysics, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, and analyzed on the premises by an appropriately trained technician. The samples were received in January 2012 and assayed for total fatty acid composition using high-throughput robotic direct methylation coupled with fast gas–liquid chromatography, which was developed and validated by the referred institution, with a inter-assay variance of $< 0.5\%$ (Masood and Salem, 2008; Lin et al., 2012).

2.5. Statistical analysis

The data were entered using duplicate typing, followed by an analysis of data consistency. Both procedures were conducted using Census and Survey Processing System (CSPro) software, version 4.1.002.

We first analyzed the prevalence distribution of the two outcomes (SR or MDE) according to key confounding variables that were previously determined in a theoretical model. In the first stage, the distribution of each covariate was investigated for each outcome with the objective of defining categories with a higher prevalence of SR and MDE. The prevalences were compared using the chi-squared test for proportions. In the second stage, all variables with a p-value < 0.20 were included in the multiple model to build the final model for each outcome. Two independent multiple models were built including only the covariates that presented a p-value < 0.05 for each outcome.

The third stage considered the independent effect of each individual fatty acid on the two outcomes, adjusting for the variables included in the final multiple model. Fatty acid data were converted to Z scores and entered as continuous variables in the logistic regression models. Each individual fatty acid was assessed (eg, increase in Z score) for SR and MDE. An independent multiple model for each fatty acid was adjusted for key confounders that had previously been identified for the corresponding outcome. However, considering the possibility of fatty acid mobilization during early pregnancy, gestational week was entered into the model as a continuous variable to adjust the fatty acid levels. The strengths of the associations were measured using odds ratios and 95% confidence intervals. All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 19.0.

3. Results

Two hundred thirty-four women were enrolled in the study. The prevalence of SR observed in the sample was 19.6% ($n=46$). A higher prevalence of SR was observed in women with ≥ 2 children (38.2%), women who were single (36.0%), women with current alcohol consumption (31.9%), women with the lowest monthly per capita family income (29.5%), and women with home crowding > 2 persons per room (28.2%) (Table 1). The prevalence of MDE observed in the sample was 17.0% ($n=40$), and a greater prevalence was observed among smokers (44.4%), single women (36%), women with ≥2 children (24.4%), women with ≤1 close relative (24.0%), women with the lowest monthly per capita family income (23.6%), and women of the youngest age (19.8%) (Table 1).

In the multiple for SR, the variables that remained associated with this outcome were marital status and parity, which increased the chances for occurrence of SR by 2.98-fold (95% CI: 1.16-2.72) and 5.82-fold (95% CI: 2.15–12.34), respectively (Data not shown). In the final model for MDE, the variables that remained associated with MDE were marital status (OR=3.07; 95% CI: 1.19-7.92), current smoking status (OR=5.42; 95% CI: 1.89-15.50), and number of close relatives (OR=2.32; 95% CI: 1.11-4.85) (Data not shown).

In the multiple models, each increase of standard deviation in the arachidonic acid (AA; 20:4*n*-6) or adrenic acid (AdA; 22:4n-6) level was associated with a 45% (OR=1.45; 95% CI: 1.02–2.07) or 43% (OR=1.43; 95% CI: 1.01–2.04) greater chance of SR, respectively, after controling for marital status, parity, and gestational week (Table 2). In the multiple models of MDE, each increase of one standard deviation in the AA or AdA level was associated with a 47% (OR=1.47; 95% CI: 1.03–2.10) or 59% (OR=1.59; 95% CI: 1.09–2.32) greater chances of MDE, respectively, after controling for marital status, smoking status, number of close relatives, and gestational week (Table 3).

4. Discussion

The present investigation revealed that higher blood levels of AA and AdA, two omega-6 fatty acids, were associated with a higher likelihood of SR and MDE among low-income Brazilian pregnant women studied in early pregnancy. These results remained significant after adjustment for confounders identified after multiple regression modeling with social, demographic and behavior variables. Gestational week was added into the model to control for residual effects of fatty acid mobilization that possibly occur during the first weeks of pregnancy. These results are consistent with previous findings, including associations between higher levels of AA and depressive symptoms among eldery subjects with mild cognitive impairment (Milte et al., 2011), fatty acids and increased risk of suicide deaths in the U.S. military, (Lewis et al., 2011) and seasonal variations in serum AA and suicide (De Vriese et al., 2004). To our knowledge, this is the first study that examined essential fatty acid status and SR in pregnancy, and it is the first to provide evidence that an excess of long chain n-6 PUFA in the serum may be associated with a greater likelihood of SR and MDE.

A strength of the present study is that the prevalence of mood disorders was based on a specific diagnostic instrument for mental disorders (Sheehan et al., 1998); the SR module consisted of six questions regarding suicidal behavior that were used to derive the SR variable. Another important strength of the present investigation is the use of serum composition of fatty acids, which are known to be biological markers of dietary intake (Arab and Akbar, 2002). We judged that inclusion of dietary data would be less accurate for establishing omega-3 and omega-6 status due to the difficulties in determining nutrient intake in epidemiological studies (Bingham, 2002), especially during pregnancy (Neuhouser et al., 2008). The main limitation of this investigation is the socioeconomic background of the study sample. A review of long chain essential fatty acid status in Brazilian pregnant women showed inadequate dietary DHA intake and low maternal blood DHA levels compared to the standards established in the international literature (Torres and Trugo, 2009). This discrepancy is probably the critical reason why we did not find a positive association between lower blood omega-3 levels and SR or MDE. Thus, there are limits to the external validity of this study, as our results were derived from women of low socioeconomic status

Table 1
Number of cases and prevalence of current suicide risk or major depressive episode during first trimester of pregnancy, Rio de Janeiro, (2009-2011) (n=234).

Variable	N	%	Current suicide risk[a]			Major depressive episode[a]		
			n	Prevalence (%)	P value[b]	n	Prevalence (%)	P value[b]
Monthly per capita family income (American Dollar $)[c]								
3rd tertile (≥357.65)	78	33.6	9	11.8		4	5.3	
2nd tertile (197.25-357.64)	78	33.6	14	17.9	0.020	16	20.5	0.004
1st tertile (≤ 197.24)	76	32.8	23	29.5		19	24.4	
Age (years)								
20–29	162	69.2	31	19.1	0.446	32	19.8	0.040
30–40	72	30.8	15	20.8		7	9.7	
Marital status								
Married or stable partnership	209	89.3	37	17.7	0.034	30	14.4	0.011
Single	25	10.7	9	36.0		9	36.0	
Self-reported skin color								
White	59	25.2	9	15.3	0.216	7	11.9	0.174
Non-white	175	74.8	37	21.1		32	18.3	
Education (years)								
≥9	134	57.3	25	18.7	0.388	21	15.7	0.382
≤8	100	42.7	21	21.0		18	18.0	
Smoking habit (current)								
No	216	92.3	41	19.0	0.265	31	14.4	0.004
Yes	18	7.7	5	27.8		8	44.4	
Alcohol consumption (current)								
No	187	79.9	31	16.6	0.018	31	16.6	0.546
Yes	47	20.1	15	31.9		8	17.0	
Sleeping hours at night								
≥8	152	65.0	30	19.7	0.556	27	17.8	0.338
< 8	82	35.0	16	19.5		12	14.6	
Parity								
0	88	37.6	9	10.2		9	10.2	
1	91	38.9	16	17.6	< 0.001	17	18.7	0.090
≥2	55	23.5	21	38.2		13	23.6	
Previous history of abortion								
No	177	75.6	30	16.9	0.053	28	15.8	0.334
Yes	57	24.4	16	28.1		11	19.3	
Desire to be pregnant								
Yes	99	42.3	15	15.2	0.093	16	16.2	0.502
No	135	57.7	31	23.0		23	17.0	
Work status								
Yes	159	67.9	29	18.2	0.265	22	13.8	0.068
No	75	32.1	17	22.7		17	22.7	
Home crowding (persons/dorms)								
≤2	156	66.7	24	15.4	0.017	22	14.1	0.098
> 2	78	33.3	22	28.2		17	21.8	
Pre-pregnancy BMI (kg/m²)[d]								
≤24.9	132	56.4	21	15.9	0.070	18	13.6	0.108
≥25.0	102	43.6	25	24.5		21	20.6	
Number of close relatives‡								
≥2	137	58.8	24	17.5	0.253	16	11.7	0.011
0-1	96	41.2	21	21.9		23	24.0	
Number of close friends‡								
≥2	113	48.5	18	15.9	0.135	19	16.8	0.557
0-1	120	51.5	27	22.5		20	16.7	
Reported family history of depression (first-degree relative)[e]								
No	173	74.9	34	19.7	0.538	31	17.9	0.204
Yes	58	25.1	11	19.0		7	12.1	
Reported family history of suicide (first-degree relative)[e]								
No	219	94.4	43	19.6	0.295	35	16.0	0.313
Yes	12	5.2	1	8.3		3	25.0	

[a] M.I.N.I International Neuropsychiatric Interview (DSM-IV; version 5.0.0.);
[b] Fisher exact test *P*-value refers to chi-square for proportions for all dichotomous variables. For non-dichotomous variables, Yates correction was applied;
[c] Two missing values for monthly per capita family income;
[d] Body mass index (BMI) classification according to the World Health Organization (1995); One individual was missing values for both the close friends and close relatives variables;
[e] There were three answers of 'I don't know' for both 'reported family history of depression' and 'reported family history of suicide'.

who visited a public health center in the city of Rio de Janeiro and may not be generalizable to women of higher education or socio-economic status.

AA and AdA are nutritionally fatty acids, primarilly obtained from animal products consumed in the diet or converted from the nutritionally essential linoleic acid (18:2 n-6), which occurs mostly in the liver (Salem et al., 1999; Rapoport et al., 2007). AA and DHA (22:6 *n*-3) are the main lipid components of the central nervous system (CNS) and are indispensable to normal development and biochemistry (Chen et al., 2008). During the last century, populations exposed to a Western dietary pattern have experienced a shift in their fat consumption towards higher intake from

Table 2
Serum fatty acid status and adjusted odds ratios of current suicide risk during first trimester of pregnancy, Rio de Janeiro, 2009-2011 (n=234).

Fatty acids[a]		Current suicide risk		Unadjusted	Adjusted[c]
		No (*n*=188) Mean (SD)	Yes (*n*=46) Mean (SD)	Odds ratio (95% CI)[b]	Odds ratio (95% CI)[b]
Omega-6 polyunsaturated fatty acids (%)					
LA	18:2 *n*-6	31.00 (3.43)	30.44 (3.68)	0.85 (0.62–1.17)	0.78 (0.56–1.08)
	18:3 *n*-6	0.33 (0.13)	0.37 (0.14)	1.30 (0.95–1.77)	1.26 (0.91–1.74)
	20:2 *n*-6	0.32 (0.07)	0.31 (0.06)	0.87 (0.60–1.25)	0.80 (0.53–1.21)
	20:3 *n*-6	1.88 (0.46)	1.94 (0.44)	1.12 (0.82–1.53)	1.21 (0.86–1.69)
AA	20:4 *n*-6	9.17 (1.56)	9.62 (1.89)	1.34 (0.96–1.87)	**1.45 (1.02–2.07)**
AdA	22:4 *n*-6	0.39 (0.09)	0.41 (0.10)	1.29 (0.93–1.79)	**1.43 (1.01–2.04)**
	22:5 *n*-6	0.39 (0.09)	0.41 (0.10)	1.10 (0.80–1.51)	1.29 (0.91–1.83)
	n-6 HUFA	78.07 (3.89)	78.76 (3.85)	1.22 (0.85–1.77)	1.17 (0.81–1.69)
Omega–3 polyunsaturated fatty acids (%)					
	18:3 *n*-3	0.63 (0.14)	0.62 (0.15)	0.96 (0.70–1.32)	0.80 (0.56–1.14)
EPA	20:5 *n*-3	0.42 (0.22)	0.44 (0.20)	1.09 (0.80–1.49)	1.10 (0.78–1.56)
DPA	22:5 *n*-3	0.53 (0.11)	0.55 (0.14)	1.20 (0.86–1.66)	1.23 (0.87–1.73)
DHA	22:6 *n*-3	2.46 (0.56)	2.42 (0.58)	0.94 (0.66–1.32)	1.07 (0.75–1.52)
	n-3 HUFA	21.93 (3.89)	21.24 (3.85)	0.82 (0.57–1.80)	0.85 (0.59–1.23)
Monounsaturated fatty acids (%)					
	16:1 *n*-7	1.63 (0.60)	1.67 (0.57)	1.07 (0.79–1.45)	1.08 (0.79–1.48)
	18:1 n-9	15.98 (1.81)	15.91 (1.75)	0.96 (0.70–1.34)	1.06 (0.75–1.50)
	18:1 *n*-7	1.69 (0.21)	1.70 (0.25)	1.04 (0.75–1.44)	1.24 (0.87–1.76)
	20:1 *n*-9	0.15 (0.03)	0.15 (0.03)	0.90 (0.63–1.29)	0.99 (0.66–1.47)
	24:1 *n*-9	1.12 (0.19)	1.12 (0.20)	0.99 (0.72–1.36)	1.16 (0.81–1.64)
	Total	20.58 (2.32)	20.56 (2.11)	0.99 (0.72–1.37)	1.11 (0.79–1.57)
Saturated fatty acids (%)					
	14:0	0.68 (0.26)	0.66 (0.26)	0.95 (0.69–1.29)	0.89 (0.63–1.25)
	16:0	21.90 (1.75)	21.93 (1.72)	1.01 (0.74–1.39)	0.96 (0.68–1.35)
	18:0	7.47 (0.68)	7.43 (0.62)	0.93 (0.66–1.31)	0.92 (0.62–1.35)
	20:0	0.31 (0.05)	0.32 (0.05)	1.12 (0.82–1.54)	1.34 (0.93–1.91)
	22:0	0.85 (0.13)	0.87 (0.20)	1.19 (0.87–1.61)	1.17 (0.85–1.62)
	24:0	0.73 (0.12)	0.74 (0.16)	1.12 (0.81–1.55)	1.08 (0.77–1.50)
	Total	31.94 (1.68)	31.95 (1.49)	1.01 (0.73–1.39)	0.94 (0.67–1.32)

[a] Fatty acids are expressed as percentage of total serum fatty acids.
[b] Odds ratios of current suicide risk per standard deviation for each fatty acids,
[c] adjusted by parity, marital status and gestational week, using binary logistic regression; Abbreviations: SD=standard deviation; CI=confidence interval; LA=linolenic acid; AA=arachidonic acid; AdA=adrenic acid; HUFA=highly unsaturated fatty acid; EPA=eicosapentaenoic acid; DPA=docosapentaenoic acid; DHA=docosahexaenoic acid.

processed food, mostly manufacturated with vegetable oils rich in omega-6 fatty acids such as soybean, corn and sunflower oils, and significantly lower intake of dietary sources of omega-3 fatty acids (e.g., oily fish, green vegetables and nuts) (Blasbalg et al., 2011). SR and MDE are both linked to the neurobiology of inflammatory responses in the brain (Erhardt et al., 2012; Maes et al., 2012; Maes, 1995). AA is a substrate for the synthesis of inflammatory cytokines (Lotrich et al., 2012). The long chain omega-3 fatty acids DHA and eicosapentaenoic acid (EPA; 20:5 *n*3) have anti-inflammatory and inflammation-resolving properties (McNamara et al., 2010; Calder, 2008). Although the present investigation does not provide evidence to support the hypothesis of omega-3 insufficiency as a possible risk for mood disorders, our findings suggest that higher AA and AdA status may be considered to be a risk factor for SR and MDE in early pregnancy.

Several biological mechanisms are consistent with the association between higher AA and AdA and SR and MDE. Excessive serum levels of AA and its cascade were first implicated in the pathogenesis of affective disorders in 1989 (Hibbeln et al., 1989), and the net overlapping effects of at least three mood stabilizers are a decreased turnover of AA, as well as decreased brain cyclo-oxygenase-2 and prostaglandin E(2) (Bazinet, 2009). Two randomized clincal trials reported that inhibition of cyclo-oxygenase-2 with Celebrex significantly reduced depressive symptoms (Akhondzadeh et al., 2009). A critical role for excess prostaglandin E(2) has been further evaluated in animal models of depression (Song et al., 2009) and stress related to social defeat (Tanaka et al., 2012). An evaluation of fatty acid compositions in adolescent brains on autospy found that suicide victims had a possible selective abnormality in AA metabolism; the victims did not exhibit the normal age-related decrease in AdA composition and the AA to DHA ratio (McNamara et al., 2009). Another putative link between diet, serum levels of n-6 long chain PUFA and mood disorders is the endocanobinnoid system of the CNS, which is involved in regulating physiological and pathophysiological aspects of mood, in addition to other functions (DiLeone 2011). The two principal endocannabinoids - anandamide (AEA) and 2-arachidonoylglycerol (2-AG)—are structurally derived from essential n-6 fatty acids, mainly AA, and have cellular signaling functions in the modulation of neurotransmitter release that have been implicated in the pathophysiology of suicide and depression (Vinod and Hungund, 2006). Selective dietary elevation of LA in animals following pregnancy resulted in a higher content of n-6 PUFA in the brain, including AA and ADA, and brain 2-AG (Alvheim et al., 2012).

In recent years, various fish oil suplementation trials in pregnancy have focused on the treatment or prevention of maternal depression (Freeman et al., 2008; Su et al., 2008; Rees et al., 2008; Makrides et al., 2010). Despite the plausible neurotrophic effect of n-3 PUFA on mental health, only one study reported a positive effect of DHA and EPA over placebo during pregnancy (Su et al., 2008). However, intervention trials for depressive disorders are difficult to conduct for many reasons; subjects with sufficient depresive symptoms must be ethically treated, and prevention trials must be large enough for adequate statistical power and placebo responses.

Our investigation using an individual structured psychiatric interview revealed that the prevalence of SR (19.6%) and MDE (17.0%) is high among low-income Brazilian women in early pregnancy (≤13 weeks gestation). Reported prevalences of

Table 3
Serum fatty acid status and adjusted odds ratios of major depressive episode during first trimester of pregnancy, Rio de Janeiro, 2009-2011 (n=234).

Fatty acids[a]		Major depressive episode		Unadjusted	Adjusted[c]
		No (n=194) Mean (SD)	Yes (n=40) Mean (SD)	Odds ratio (95% CI)[b]	Odds ratio (95% CI)[b]
Omega-6 polyunsaturated fatty acids (%)					
LA	18:2 *n*-6	30.99 (3.41)	30.39 (3.81)	0.84 (0.60–1.18)	0.74 (0.52–1.06)
	18:3 *n*-6	0.34 (0.14)	0.36 (0.14)	1.15 (0.82–1.60)	1.13 (0.78–1.62)
	20:2 *n*-6	0.32 (0.07)	0.31 (0.06)	0.75 (0.50–1.12)	0.67 (0.42–1.05)
	20:3 *n*-6	1.91 (0.48)	1.81 (0.35)	0.81 (0.57–1.15)	0.78 (0.53–1.15)
AA	20:4 *n*-6	9.16 (1.57)	9.73 (1.87)	1.44 (1.01–2.06)	**1.47 (1.03–2.10)**
AdA	22:4 *n*-6	0.38 (0.09)	0.41 (0.09)	1.39 (0.99–1.94)	**1.59 (1.09–2.32)**
	22:5 *n*-6	0.36 (0.13)	0.36 (0.12)	1.02 (0.73–1.43)	1.12 (0.78–1.63)
	n-6 HUFA	78.01 (3.88)	79.15 (3.80)	1.43 (0.94–2.18)	1.25 (0.82–1.90)
Omega–3 polyunsaturated fatty acids (%)					
	18:3 *n*-3	0.63 (0.14)	0.61 (0.13)	0.87 (0.61–1.23)	0.80 (0.56–1.14)
EPA	20:5 *n*-3	0.43 (0.22)	0.41 (0.21)	0.93 (0.64–1.35)	1.02 (0.69–1.49)
DPA	22:5 *n*-3	0.53 (0.11)	0.53 (0.11)	0.95 (0.66–1.37)	1.01 (0.70–1.47)
DHA	22:6 *n*-3	2.46 (0.54)	2.40 (0.65)	0.89 (0.61–1.28)	1.06 (0.72–1.55)
	n-3 HUFA	21.99 (3.88)	20.85 (3.80)	0.70 (0.46–1.06)	0.80 (0.52–1.21)
Monounsaturated fatty acids (%)					
	16:1 *n*-7	1.62 (0.59)	1.70 (0.62)	1.13 (0.83–1.55)	1.18 (0.84–1.65)
	18:1 *n*-9	15.96 (1.79)	15.98 (1.84)	1.01 (0.72–1.43)	1.05 (0.72–1.52)
	18:1 *n*-7	1.69 (0.21)	1.72 (0.24)	1.18 (0.84–1.66)	1.22 (0.84–1.78)
	20:1 *n*-9	0.15 (0.03)	0.15 (0.03)	0.84 (0.57–1.24)	0.85 (0.56–1.29)
	24:1 *n*-9	1.12 (0.19)	1.16 (0.20)	1.28 (0.91–1.80)	1.38 (0.94–2.01)
	Total	20.54 (2.25)	20.72 (2.42)	1.08 (0.77–1.52)	1.14 (0.79–1.64)
Saturated fatty acids (%)					
	14:0	0.68 (0.27)	0.64 (0.24)	0.85 (0.60–1.21)	0.87 (0.60–1.28)
	16:0	21.88 (1.73)	22.05 (1.80)	1.09 (0.79–1.52)	1.22 (0.85–1.75)
	18:0	7.48 (0.68)	7.37 (0.62)	0.84 (0.58–1.20)	0.76 (0.51–1.13)
	20:0	0.32 (0.05)	0.32 (0.05)	1.06 (0.76–1.49)	1.19 (0.82–1.72)
	22:0	0.85 (0.14)	0.85 (0.17)	1.03 (0.74–1.44)	1.07 (0.75–1.52)
	24:0	0.73 (0.12)	0.72 (0.17)	0.94 (0.66–1.34)	0.94 (0.65–1.36)
	Total	31.94 (1.67)	31.95 (1.54)	1.01 (0.72–1.41)	1.10 (0.76–1.58)

[a] Fatty acids are expressed as percentage of total serum fatty acids; Bold typeface indicate significant items;
[b] Odds ratios of major depressive episode per standard deviation for each fatty acids,
[c] adjusted by marital status, current smoking habit, close relatives and gestational week, using binary logistic regression; Abbreviations: SD=standard deviation; CI=confidence interval; LA=linolenic acid; AA=arachidonic acid; AdA=adrenic acid; HUFA=highly unsaturated fatty acid; EPA=eicosapentaenoic acid; DPA=docosapentaenoic acid; DHA=docosahexaenoic acid.

maternal depression are higher in developing countries than in developed countries. A recent systematic review conducted by Fisher et al. (2012) reported a mean prevalence of prenatal depression, summarized across 17 low- to middle-income countries, of 15.6% (95% CI 15.4–15.9) (Fisher et al., 2012). Our findings regarding SR are in line with a cross-sectional study carried out by Pinheiro et al. (2012) that focused on pregnant teenagers attending public pre-natal care centers in a southern city of Brazil (Pinheiro et al., 2012). In this study, the SR was 13.3% and the MDE was 17.8%. Other studies on SR in pregnancy have focused on unqiue suicide ideation, and reported prevalences ranged from 2.9% (Gavin et al., 2011) to 14.6% (Lindahl et al., 2005). The main reason for this difference is that the MINI defines SR as the sum of several components (thoughts of death, self-harm and suicidal ideation, and suicide attempt [past and recent]), so the results are not restricted to suicidal ideation by self-reported scales.

Our study provides evidence that SR and MDE are common public health and clinical problems among low-income Brazilian women in early pregnancy. Moreover, this is the first epidemiological study on mood disorders among Brazilian pregnant women to investigate blood fatty acid levels, and it is the first to provide evidence that an excess of long chain n-6 PUFA in serum might be associated with a greater likelihood of SR and MDE.

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Conflict of interest

J. S. Vaz, A. E. Nardi, G. Kac, J.R. Hibbeln have no conflicts of interests.

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