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## Association of Antepartum Suicidal Ideation during the Third Trimester with Infant Birth Weight and Gestational Age at Delivery

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### Abstract

Antepartum suicidal behaviors, including suicidal ideation and attempts, are a leading cause of maternal injury and death worldwide. Previous research has not investigated the association between suicidal ideation during pregnancy and perinatal complications. The objective of our study was to evaluate the relationship of antepartum suicidal ideation with low infant birthweight, small for gestational age, and preterm birth. A cohort study was conducted among 1,108 pregnant women receiving prenatal care in Lima, Peru. Suicidal ideation was measured using the Patient Health Questionnaire-9 during pregnancy, and birth outcomes were extracted from patients' medical records. Linear regression procedures were used to investigate associations between suicidal ideation and pregnancy outcomes. Multivariable logistic regressions were used to estimate odds ratios (OR) and 95% confidence intervals (95% CI). The prevalence of suicidal ideation was 8.7%, preterm delivery was 5.7%, low birthweight was 4.4%, and small for gestational age was 3.4%. In a fully adjusted model, infant birthweight was 94.2 grams lower for mothers with antepartum suicidal ideation (95% CI: -183.0, -5.5,  $p=0.037$ ) compared with those with no suicidal ideation. After adjusting for confounders including depression, participants with suicidal ideation had a nearly four-fold increased odds of delivering a small for gestational age infant (OR: 3.73; 95% CI: 1.59 – 8.74). These findings suggest women's suicidal ideation during pregnancy is associated with adverse perinatal outcomes, especially low infant birthweight.

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## Introduction

A recent report from the World Health Organization (WHO) estimates that over 800,000 individuals die by suicide each year, resulting in an annual global age-standardized suicide rate of 11.4 per 100,000 persons with 75.5% of suicides occurring in low- and middle-income countries (World Health Organization, 2014). For each completed suicide, many more suicide attempts exist that may result in severe injury (Nock et al., 2008). Of note, an accumulating body of evidence now implicates suicidal ideation as a precursor and important risk factor of later suicide attempts and completed suicide (Nock, et al., 2008). Although rates of maternal deaths attributable to obstetrically related events, such as preeclampsia, infection, and hemorrhage, have declined over the past two decades, rates of maternal deaths attributable to suicide have remained unchanged (Palladino, Singh, Campbell, Flynn, & Gold, 2011; Shadigian and Bauer, 2005). Furthermore, recent research suggests that suicidal ideation is a relatively common complication of pregnancy worldwide (Gelaye, Kajeepeta, & Williams, 2016; Gentile, 2011). However, few studies have assessed the relationship between experiences of suicidal ideation in pregnancy with perinatal outcomes (Hodgkinson, Colantuoni, Roberts, Berg-Cross, & Belcher, 2010).

Previous studies show that antenatal mental health is associated with adverse pregnancy outcomes, including perinatal complications (Hollins, 2007). Common perinatal complications include low birthweight, preterm birth, and infants born small for their gestational age. Globally, approximately 13 million infants are born prematurely, and the preterm birth rate in South America is estimated as 7.9% (Lawn et al., 2010). Low birthweight is common among premature newborns, and both premature birth and low birthweight are leading causes of neonatal morbidity and mortality (Branum and Schoendorf, 2002). Infants born small for gestational age are at increased likelihood of neonatal mortality (Boguszewski et al., 2011). Later in life, infants with delivery complications have an increased risk of adverse health outcomes including cardiovascular disease (Abitbol and Rodriguez, 2012; Kerkhof, Breukhoven, Leunissen, Willemsen, & Hokken-Koelega, 2012), obesity (Gaskins et al., 2010), diabetes (Li et al., 2014), asthma (Sonnenschein-van der Voort et al., 2014), cognitive impairment (de Bie, Oostrom, & Delemarre-van de Waal, 2010; Pyhala et al., 2014), and depression (Loret de Mola, de Franca, Quevedo Lde, & Horta, 2014). Given that (1) suicide during pregnancy is one of the leading causes of maternal mortality (Oates, 2003; World Health Organization, 2008), and (2) there is an existing gap in research investigating perinatal complications associated with suicidal ideation during pregnancy (Fuhr et al., 2014; World Health Organization, 2009), we evaluated the association between antepartum suicidal ideation and the odds of low infant birthweight, small for gestational age, and preterm delivery in a well characterized cohort of pregnant women.

## Methods

### Study Population

Our cohort included pregnant women receiving prenatal care from the Instituto Nacional Materno Perinatal (INMP) in Lima, Peru between February 2013 and May 2014. INMP is

the primary reference establishment for maternal and perinatal care operated by the Ministry of Health of the Peruvian government. Eligible participants were pregnant women between 24 and 28 gestational weeks, 18 years or older, and who spoke and understood Spanish. Given that the main objective of the primary study was to calculate the incidence of gestational diabetes, women were excluded if they already had a diagnosis of diabetes. A total of 1,108 participants were included in the analysis. All participants provided written informed consent. Study procedures were approved by the Institutional Review Board at the INMP, Lima, Peru and the Human Research Administration Office at the Harvard T. H. Chan School of Public Health, Boston, Massachusetts, USA.

### Depression and Suicidal Ideation Assessment

Depression and suicidal ideation was assessed using the Spanish-language Patient Health Questionnaire-9 (PHQ-9) (Kroenke, Spitzer, & Williams, 2001; Wulsin, Somoza, & Heck, 2002). The PHQ-9 is a 9-item screening tool for depression and suicidal ideation which has previously been validated in this population (Zhong, Gelaye, Fann, Sanchez, & Williams, 2014). The PHQ-9 assesses depressive symptoms on the 14 days prior to the assessment. Scores of 0–3 were assigned to each of the nine questions according to responses “not at all,” “several days,” “more than half the days,” or “nearly every day.” Suicidal ideation was based on the PHQ-9 question asking patients about “thoughts that you would be better off dead or of hurting yourself in some way.” Participants who responded with “several days,” “more than half the days,” or “nearly every day” were considered to have suicidal ideation. The suicidal ideation question was not included in the total score for depression, and the first 8 questions (PHQ-8) were used to calculate a depression score. Participants with a PHQ-8 score of  $\geq 10$  were categorized as having depression, similar to the cutoff for the PHQ-9 (Kroenke, Spitzer, Williams, & Lowe, 2010; Kroenke et al., 2009). Use of the PHQ-8 questionnaire to measure depression status has been shown minimally influence mean scores, and diagnostic cut points, and scale performance as compared with use of PHQ-9 (Kroenke, et al., 2010; Kroenke, et al., 2009).

### Pregnancy Outcomes

Pregnancy outcome variables included birthweight and gestational age at delivery. Information was extracted from patients’ medical records. The diagnosis of preterm delivery was made using guidelines from the American College of Obstetricians and Gynecologists (*ACOG technical bulletin. Preterm labor.*, 1995). Gestational age was based on date of last menstrual period and confirmed by an ultrasound during perinatal visits before 20 weeks. Preterm delivery was defined as delivery prior to the completion of 37 gestational weeks. Small for gestational age was defined as sex-specific birthweight <10th percentile of birthweight by gestational age (Lubchenco, Hansman, Dressler, & Boyd, 1963).

### Sociodemographic Characteristics

Participants completed structured interviews that collected information on sociodemographic characteristics. Participants’ age was categorized as: 18–20, 20–29, 30–34, and  $\geq 35$  years old. Other covariates included educational attainment ( $\leq 12$  vs.  $>12$  years of education); ethnicity (Mestizo vs. others); marital status (married/living with partner vs. others); employment status (employed vs. not employed); access to basic foods (hard vs. not very

hard); parity (nulliparous vs. multiparous); planned pregnancy (yes vs. no); prenatal vitamin intake; smoking during pregnancy; alcohol use during pregnancy; pre-pregnancy self-reported body mass index (BMI) (<18.5, 18.5–24.9, 25–29.9, >30 kg/m<sup>2</sup>) and early pregnancy measured BMI; self-reported health status during the last year and during pregnancy (good vs. poor); subsequent preeclampsia; gestational age at interview and at delivery (weeks); preterm delivery (no, yes, unknown); infant birthweight (grams); low birthweight (no vs. yes); and infant weight for gestational age (AGA = appropriate for gestational age; LGA = large for gestational age; SGA = small for gestational age).

### Statistical Analysis

Demographic and reproductive characteristics of participants were first examined. Mean and standard deviations (SD) were calculated for continuous variables. Categorical variables were expressed as numbers (percent, %). Chi-squared tests were used to evaluate the differences in the distribution of categorical variables. Differences in mean were evaluated using Student's t-test statistics. Multivariable linear regression procedures were used to estimate mean differences in birthweight and gestation age at delivery, after adjusting for confounders, for women with suicidal ideation as compared to those without.

Finally, multivariable logistic regression procedures were used to estimate odds ratios (OR) and 95% confidence intervals (95% CI) for suicidal ideation in relation to preterm delivery, small for gestational age, and low birthweight. Covariates were entered into each model individually, and adjusted and unadjusted ORs were compared to assess confounding. The final adjusted models included variables that were previously identified as potential confounders or altered the adjusted OR by at least 10%. All reported P-values are two sided with a statistical significance set at 0.05. Statistical analyses were performed using SPSS (IBM SPSS v22.0, Chicago, IL, USA).

### Results

The prevalence of suicidal ideation in our study cohort was 8.7%, preterm delivery 5.7%, low birthweight 4.4%, and small for gestational age 3.4%. Sociodemographic and reproductive characteristics of the study participants are presented in Table 1. The average age of study participants was 28.8 years (SD=6.1); the average infant birthweight was 3,404 grams (SD=495); and the average gestational age at delivery was 38.9 weeks (SD=1.5). The majority of participants had 12 years of education (56.3%), were married or living with a partner (85.9%), Mestizo (98%), multiparous (66.7%), and reported good health status both during their pregnancy (52.9%) and in the past year (66.1%). Women who experienced suicidal ideation were more likely to have less than 12 years of education, have difficulty accessing the basics including food, and have an unplanned pregnancy (Table 1). Participants with suicidal ideation also were more likely to have depression (38.5%) compared to those without suicidal ideation (6.9%).

Average infant birthweight was 96.5 grams lower for participants with suicidal ideation (95% CI: -181.7, -11.4, p=0.026) compared to those without suicidal ideation after adjusting for potential confounders (Table 2). After further adjustment for depression, infant birthweight was 94.2 grams lower for women with suicidal ideation (95% CI: -183.0, -5.5,

p=0.037) compared with those without. In a fully adjusted model, gestational age at delivery decreased by 0.07 weeks for participants with suicidal ideation; however, the association was not significant (p=0.688; Table 2).

In the fully adjusted model, participants with suicidal ideation had 3.73-fold increased odds of small for gestational age infants (OR: 3.73, 95% CI: 1.59–8.74) compared to participants with no suicidal ideation. Participants with suicidal ideation did not have a statistically significant increased odds of preterm delivery or low birthweight infants compared to participants without suicidal ideation (Table 3).

## Discussion

We found that infant birthweight was 94.2 grams lower for participants with suicidal ideation (95%CI: -183.0, -5.5, p=0.037) compared with those without suicidal ideation. Gestational age at delivery decreased by 0.07 weeks for women with suicidal ideation, although the association was not statistically significant. After adjusting for confounders, women with suicidal ideation had 3.73-fold increased odds of small for gestational age infants (OR: 3.73, 95% CI: 1.59–8.74) compared to women without suicidal ideation.

Our study is one of the first to examine the association between suicidal ideation and pregnancy outcomes, including gestational age, infant birthweight, and preterm birth. However, we can tentatively compare our results to studies examining maternal mental health and pregnancy outcomes. A study on pregnant adolescents showed that those with depression and suicidal attempt or ideation had a greater risk of delivering low birthweight infants compared to those with depression only or no depression and no suicidal behaviors (Hodgkinson, Colantuoni, Roberts, Berg-Cross, & Belcher, 2010). A recent meta-analysis of 30 articles found premature delivery was significantly associated with maternal depression (OR= 1.37; 95% CI, 1.04 to 1.81; P = .024). However, low birthweight and gestational age were not significantly associated with maternal depression status (Grigoriadis et al., 2013). In a Taiwanese population-based study, antepartum bipolar disorder was associated with low birthweight, preterm birth, and small for gestational age infants compared to women with no mental illness (Lee and Lin, 2010). In a retrospective cohort study in Japan, pregnant women with any mental disorders had a significantly shorter gestational age ( $39.2 \pm 0.2$  vs  $39.8 \pm 0.1$  weeks,  $P = 0.003$ ), and lower birthweight ( $2993.0 \pm 56.7$  vs  $3152.4 \pm 23.6$  g,  $P = 0.010$ ) compared to controls (Hironaka et al., 2011). Maternal mental disorders, including depression, have been previously associated with pregnancy outcomes.

The strengths of our study include a relatively large sample size, a questionnaire which has been validated in both English and Spanish, and a well-trained interview staff. However, some limitations are also present. Suicidal ideation was diagnosed based on self-report in the past two weeks, so it is possible that some participants may not have reported accurately or may not have recalled these thoughts. Additionally, suicidal ideation was measured by a single question of the PHQ-9. Use of a single question for screening may lead to misclassification of study participants and decreased statistical power to detect an association between suicidal ideation and birth outcomes. Furthermore, our study was conducted among urban dwelling low-income women, so we must exercise caution when

extrapolating our results to other populations. Lastly, we cannot rule out the possibility of unmeasured confounding by characteristics that may influence the association between suicidal ideation and birth outcomes. To that end, we conducted a rigorous statistical analysis to control from confounding from sociodemographic characteristics (i.e. parity, access to foods, planned pregnancy, alcohol intake) and mental health characteristics (i.e. depression, and self-reported health status) of our population.

Antepartum suicidal ideation is a common complication during pregnancy and is associated with numerous adverse maternal and fetal outcomes. Our study demonstrates the association between the presence of suicidal ideation and lower infant birthweights. Further studies are warranted to confirm the association in diverse populations. Pending replication, findings from this study suggest increased screen for depression and suicidal ideation during pregnancy are needed in places where there is appropriate treatment and support. Diagnosis during pregnancy is especially importance since suicidal ideation is a precursor and risk factor of later suicide attempts and completed suicide. Clinicians should implement protocols to identify high risk pregnant women and provide appropriate intervention and mental health resources.

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**Table 1:**

Sociodemographic and reproductive characteristics of the study participants (N = 1,108)

Characteristics	All participants (N = 1,108)		PHQ-9 Suicidal Ideation				P-value <sup>c</sup>
			No (N = 1,012)		Yes (N = 96)		
	n	%	n	%	n	%	
Age (years) <sup>a</sup>	28.8 ± 6.1		28.8 ± 6.1		28.6 ± 6.4		0.75
Age (years)							
18–20	45	4.1	40	4.0	5	5.2	0.67
20–29	570	51.4	525	51.9	45	46.9	
30–34	266	24.0	239	23.6	27	28.1	
35	227	20.5	208	20.5	19	19.8	
Education (years) <sup>a</sup>	12.2 ± 2.4		12.3 ± 2.4		11.5 ± 2.3		<b>0.003</b>
Education (years)							
12	624	56.3	554	54.7	70	72.9	<b>0.001</b>
>12	484	43.7	458	45.3	26	27.1	
Mestizo (race)	1086	98.0	994	98.2	92	95.8	0.21
Married/living with a partner	952	85.9	876	86.6	76	79.2	0.14
Employed	354	32.0	329	32.5	25	26.0	0.19
Access to basic foods							
Hard	541	48.8	483	47.7	58	60.4	<b>0.02</b>
Not very hard	567	51.2	529	52.3	38	39.6	
Nulliparous	369	33.3	346	34.2	23	24.0	<b>0.04</b>
Planned pregnancy	500	45.1	470	46.4	30	31.3	<b>0.004</b>
Prenatal vitamin intake	865	78.1	796	78.7	69	71.9	0.13
Smoking during pregnancy	11	1.0	10	1.0	1	1.0	0.96
Alcohol use during pregnancy	30	2.7	24	2.4	6	6.3	<b>0.03</b>
Pre-pregnancy BMI (kg/m <sup>2</sup> )	25.2 ± 4.0		25.2 ± 3.9		25.1 ± 4.2		0.82
BMI at interview (kg/m <sup>2</sup> )	27.7 ± 3.8		27.7 ± 3.7		27.6 ± 4.1		0.83
Self-reported health (last year)							
Good	732	66.1	684	67.6	48	50.0	<b>0.001</b>
Poor	376	33.9	328	32.4	48	50.0	
Self-reported health status during pregnancy							
Good	583	52.9	551	54.5	32	33.3	<b>&lt;0.001</b>
Poor	525	46.1	461	45.6	64	66.7	
Depression <sup>b</sup>	107	9.7	70	6.9	37	38.5	<b>&lt;0.001</b>
Subsequent preeclampsia/toxemia	93	8.4	86	8.4	7	7.3	0.68
Gestational age at interview <sup>a</sup>	25.5 ± 1.2		25.5 ± 1.2		25.7 ± 1.3		0.17
Gestational age at delivery <sup>a</sup>	38.9 ± 1.5		38.9 ± 1.5		38.8 ± 1.4		0.35
PTD (<37 weeks gestational age)							
No	1036	93.5	947	93.6	89	92.7	0.71

Characteristics	All participants (N= 1,108)		PHQ-9 Suicidal Ideation				P-value <sup>c</sup>
			No (N = 1,012)		Yes (N = 96)		
	n	%	n	%	n	%	
Yes	63	5.7	57	5.6	6	6.3	
Unknown	9	0.8	8	0.8	1	1.0	
Infant birthweight (grams) <sup>a</sup>	3404 ± 495		3417 ± 492		3267 ± 511		<b>0.005</b>
Low birthweight (<2500 grams)							
No	1059	95.6	971	96.0	88	91.7	0.051
Yes	49	4.4	41	4.1	8	8.3	
Infant weight for gestational age							
AGA	861	77.7	790	78.1	71	74.0	<b>0.010</b>
LGA	200	18.1	185	18.3	15	15.6	
SGA	38	3.4	29	2.9	9	9.4	
Unknown	9	0.8	8	0.8	1	1.0	

Due to missing data, percentages may not add up to 100%.

Abbreviations: BMI = Body Mass Index; PTD = preterm delivery; AGA = Appropriate for gestational age; LGA = large for gestational age; SGA = small for gestational age

<sup>a</sup>: Mean ± SD (standard deviation)

<sup>b</sup>: Depression was defined as PHQ-8 score ≥ 10

<sup>c</sup>: For continuous variables, P-value calculated using Student T-Test; for categorical variables, P-value was calculated using Chi-square test or Fisher exact test

**Table 2.**

Multivariate linear regression of association of maternal suicidal ideation during middle pregnancy with gestational age at delivery and birth weight, with robust variance.

Suicidal ideation	N	Adjusted $\beta^*$ (95% CI)	P-value	Adjusted $\beta^{***}$ (95% CI)	P-value
<i>Gestational age at delivery (wks)</i>					
No	1004	Reference		Reference	
Yes	95	-0.09 (-0.39, 0.22)	0.579	-0.07 (-0.40, 0.27)	0.688
<i>Infant birthweight (grams)</i>					
No	1012	Reference		Reference	
Yes	96	-96.5 (-181.7, -11.4) <sup>1</sup>	<b>0.026</b>	-94.2 (-183.0, -5.5) <sup>2</sup>	<b>0.037</b>

\* Adjusted for maternal nulliparity (Y/N), access to basic food (Y/N), planned pregnancy (Y/N), alcohol intake during pregnancy (Y/N), and self-reported health status (good/poor).

\*\* Adjusted for maternal nulliparity (Y/N), access to basic food (Y/N), planned pregnancy (Y/N), alcohol intake during pregnancy (Y/N), self-reported health status (good/poor) and depression status (PHQ-8).

Association of gestational outcomes of preterm delivery, low infant birthweight or small for gestational age with maternal suicidal ideation during pregnancy

**Table 3.**

Suicidal ideation	N (%)	N (%)	N (%)	Adjusted OR* (95% CI)	Adjusted OR** (95% CI)
	<i>No PTD (N=1036)</i>		<i>Yes PTD (N=63)</i>		
No suicidal ideation	947 (91.4)	57 (90.5)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes suicidal ideation	89 (8.6)	6 (9.5)	0.99 (0.41–2.40)	0.98 (0.39–2.47)	
	<i>No SGA (N=1061)</i>		<i>Yes SGA (N=38)</i>		
No suicidal ideation	975 (91.9)	29 (76.3)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes suicidal ideation	86 (8.1)	9 (23.7)	3.16 (1.41–7.07)	3.73 (1.59–8.74)	
	<i>No LBW (N=1059)</i>		<i>Yes LBW (N=49)</i>		
No suicidal ideation	971 (91.7)	41 (83.7)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes suicidal ideation	88 (8.3)	8 (16.3)	2.19 (0.73–6.62) <sup>1</sup>	2.20 (0.68–7.09) <sup>2</sup>	

Abbreviations: PTD = preterm delivery, LBW = low birth weight, SGA = small for gestational age

\* Adjusted for maternal nulliparity (Y/N), access to basic food (Y/N), planned pregnancy (Y/N), alcohol intake during pregnancy (Y/N), and self-reported health status (good/poor)

\*\* Adjusted for maternal nulliparity (Y/N), access to basic food (Y/N), planned pregnancy (Y/N), alcohol intake during pregnancy (Y/N), self-reported health status (good/poor), and depression status (PHQ-8)