Published in final edited form as:
J Matern Fetal Neonatal Med. 2015 February ; 28(3): 350–355. doi:10.3109/14767058.2014.916682.

Maternal Sleep Duration and Complaints of Vital Exhaustion during Pregnancy is Associated with Placental Abruption

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Abstract

OBJECTIVE—Sleep disorders are associated with cardiovascular complications and preterm delivery (PTD). Insufficient sleep results in metabolic alterations and increased inflammation, both known to contribute to placental abruption (abruption), a determinant of PTD. We examined associations of abruption with sleep duration and complaints of vital exhaustion.

METHODS—The study included 164 abruption cases and 160 controls in a multicenter study in Peru. Data on habitual sleep duration and vital exhaustion during the first 6 months of pregnancy were elicited during interviews conducted following delivery. Women were categorized according to short, normal and long sleep duration (≤6, 7-8 and ≥9 h); and frequency of feeling exhausted. Odds ratios (OR) and 95% confidence intervals (CI) were calculated.

RESULTS—Short and long sleep durations were associated with increased odds of abruption. The ORs of abruption in relation to short (≤6 h) and long (≥9 h) sleep duration were 2.0 (95%CI 1.1-3.7) and 2.1 (95%CI 1.1-4.1), compared with normal sleep duration (7-8 h). Complaints of vital exhaustion were also associated with abruption (OR=2.37; 95%CI 1.46-3.85), and were independent of sleep duration.

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CONFLICT OF INTEREST

The authors have no competing interests to declare.

CONCLUSION—We extend the existing literature and support the thesis that maternal sleep habits and disorders should be assessed among pregnant women.

Keywords

sleep duration; exhaustion; placental abruption; pregnancy

INTRODUCTION

Placental abruption (abruption), the premature separation of the placenta from the uterus before delivery of the fetus, is one of the most devastating complications of pregnancy that occurs in up to 1.0% of all pregnancies [1]. Multi-fetal pregnancies, coagulopathies, acquired forms of thrombophilia, uterine anomalies, abdominal trauma, hypertension, premature rupture of membranes and maternal-fetal hemorrhage, and intrauterine infections are putative risk factors for abruption [2-5]. Young and advanced maternal age, grand-multiparity, and maternal cigarette smoking have also been identified as abruption risk factors [4-5]. Pathophysiologic mechanisms thought to be linked with **abru**ption include uteroplacental underperfusion and ischemia, chronic hypoxemia, inflammation, platelet activation, and endothelial cell dysfunction. On the basis of epidemiological risk factors and what is known about abruption pathogenesis, we and others have begun to conceptualize the disorder as an “ischemic placental disorder” characterized by acute and chronic pathophysiological features [1, 6].

An estimated 50-70 million US adults report chronic sleep and wakefulness disorders, some of which are preventable [7]; and these disorders have been associated with type 2 diabetes, cardiovascular disorders, and adverse perinatal outcomes including preeclampsia [8], intrauterine growth restriction [9], and preterm delivery (PTD) [9-11]. Although causal mechanisms underlying these associations have yet to be empirically demonstrated, evidence suggests that insufficient sleep results in inflammation, platelet activation, hypercoagulation, and endothelial cell dysfunction, as well as metabolic and neuroendocrine alterations, all of which are pathophysiological processes that precede abruption. Given the scarcity of research concerning poor maternal sleep and perinatal risks, we examined the risk of placental abruption in relation to maternal nightly sleep duration and complaints of vital exhaustion among Peruvian women.

METHODS

This multicenter, population-based case-control study was conducted among women that delivered live births at the Hospital Nacional Dos de Mayo, the Instituto Nacional Materno Perinatal de Lima, and the Hospital Edgardo Rebagliati Martins in Lima, Peru, from January 2009 through July 2010. The hospitals are references hospitals that manage high risk pregnancies in Lima, Peru. Patients were attended by experienced maternal-fetal-medicine physicians. The procedures used in this study were in agreement with the protocols approved by participating institutions. All participants provided written informed consent.

Placental abruption cases were identified by daily monitoring of all new admissions to antepartum, emergency room, and labor and delivery wards of participating hospitals. Study

subjects were recruited during their hospital stay. Hospital medical records were reviewed so that clinical diagnostic signs, symptoms, and physical characteristics of abruption could be objectively confirmed; and so that other clinical diagnoses associated with late pregnancy vaginal bleeding could be excluded.

Diagnosis of placental abruption

The diagnosis of abruption was based on routine clinical examination performed by the attending physician. For the research diagnosis of abruption, we required evidence of blood clot behind the placental margin accompanied by at least two of the following signs and symptoms: 1) vaginal bleeding in late pregnancy that was not associated with placenta previa or cervical lesions; 2) uterine tenderness and/or abdominal pain; and 3) poor fetal tracings suggestive of fetal distress or stillbirth. The diagnostic protocol for abruption case definition was applied across all study sites so as to make ensure diagnostic criteria were applied uniformly. Controls were selected from eligible women that delivered at the participating institutions during the study period. Eligible controls were women who did not have a diagnosis of abruption and whose medical record review later confirmed this fact. During the study period, we enrolled 164 eligible women with abruption (participate rate = 95%) and 160 control subjects (participate rate = 92%). All participants provided written informed consent.

We used a standardized, structured questionnaire to collect data on maternal sociodemographic, medical, reproductive, and lifestyle characteristics during in-person interviews. All interviews were conducted in the hospital by trained research interviewers. Data collected during the interviews included maternal age, marital status, employment status during pregnancy, medical history, and smoking and alcohol consumption during pregnancy.

Sleep and exhaustion exposures

Through in-person interviews following delivery, maternal average nightly sleep duration during early pregnancy was ascertained by asking women the following question: “During the first 6 months of your pregnancy, how many hours per night did you sleep? Responses were reported as integers. We classified participants into three groups based on short (≤ 6hours); normal (7-8 hours); and long (≥ 9 hours) sleep duration. These categorizations were decided upon *a priori*, based on previously reported cut-points used by investigators who focused on sleep problems among pregnant women [12]. Maternal report of *vital exhaustion* in early pregnancy was ascertained by asking women: “During the first 6 months of your pregnancy, how often did you feel exhausted (except after exercise)?” Response choices were: (1) never; (2) once per month; (3) 2-3 times per month; and (4) 4 times per month; (5) every week; and (6) every day. For multivariable analyses, we collapsed responses into a dichotomous variable with “never” comprising the responses never, and “ever” comprising the all other responses. We also created an ordinal variable with the categories: (1) Never, (2) 1-3 times per month; (3) 4 times per month or weekly; and (4) daily. We limited questions to early pregnancy because this period preceded any clinical manifestation of preterm labor or premature rupture of membrane. Hence, as a result of this restriction, participants were unlikely to report changes in nightly sleep duration because of abruption-

related symptoms. Maternal and infant records were reviewed to collect detailed information concerning antepartum, labor, and delivery characteristics, as well as conditions of the newborn.

Statistical analysis

We examined the frequency distribution of maternal sociodemographic characteristics and reproductive histories according to case and control status. Initial bivariate analyses were carried out to estimate unadjusted odds ratio (OR) and 95% confidence interval (CI). Logistic regression procedures were used to simultaneously control for confounding variables while estimating the adjusted ORs and 95% CIs. We also explored the possibility of a nonlinear relation between maternal sleep duration and abruption risk using the generalized additive modeling (GAM) procedure. Confounders were defined as those factors that altered the unadjusted OR by at least 10%. Final logistic regression models included confounders, as well as those covariates of *a priori* interest (i.e., maternal age and parity). Maternal educational attainment, employment status, use of prenatal care services and prenatal vitamins, as well as maternal use of tobacco, alcohol and illicit drugs were not found to be confounders and thus were not included in final models. Effect modification (the interaction between sleep duration and exhaustion) was evaluated by including appropriate two-way interaction terms in logistic regression models. All continuous variables are presented as mean ± standard deviation (SD). All reported P-values are two-tailed. All analyses were performed using STATA 9.0 statistical software (Stata, College Station, USA).

RESULTS

Socio-demographic and reproductive characteristics of abruption cases and controls are presented in **Table 1**. Cases and controls were similar with regards to maternal age, parity, educational attainment, and employment status. Compared with controls, cases were less likely to have received prenatal care. As expected, abruption cases were more likely to deliver preterm and low birth weight infants.

Mean nightly sleep hours were 7.4 for both cases and controls. However, the prevalence of short sleep duration (≤6 hours) was 22.0% among cases and 14.4% among controls. The corresponding figures for long sleep duration (≥9 hours) were 18.9% for cases and 11.9% for controls. In bivariate analyses we noted that the odds of abruption was increased 1.90-fold for women with short sleep duration (OR=1.90; 95% CI 1.06-3.43) and 1.98-fold for women who reported long sleep duration (OR=1.98; 95% CI 1.06-3.73) as compared with women who reported sleeping 7-8 hours per night. After adjusting for confounding by maternal age, parity and pre-pregnancy weight, prenatal care and alcohol consumption during pregnancy, short sleep duration (aOR=2.01; 95% CI 1.09-3.69) and long sleep duration (aOR=2.11; 95% CI 1.09-4.09) remained associated with increased odds of abruption, compared with sleep duration of 7-8 hour (**Table 2**). When we modeled the risk of abruption in relation to maternal sleep duration expressed as a continuous variable using a generalized additive model (GAM), we noted an expected “U” shape relation between abruption risk and maternal sleep duration (**Supplemental Figure 1**). The odds of abruption

was increased by 2.4-fold among women who reported feeling a sense of vital exhaustion in early pregnancy (unrelated to exercise) (aOR=2.37; 95% CI 1.46-3.85) compared to women who did not report any symptoms (**Table 2**). These associations remained statistically significant and were of similar magnitude when both sleep duration and vital exhaustion were included in the same logistic regression model.

We next completed an exploratory analysis to assess the odds of abruption in relation to independent and joint exposure short/long sleep duration and any complaint of vital exhaustion in early pregnancy. As shown in **Table 3**, we observed some evidence suggestive of effect modification though the P-values for interaction terms were not statistically significant, likely due to small sample size. Women who reported short sleep duration and who complained of exhaustion had a 4.02-fold increased odds of placental abruption (aOR=4.02; 95% CI 1.82-8.88) as compared with women who reported sleeping 7-8 hours and who had no complaints of exhaustion. Of note, women who reported sleeping long durations and who complained of vital exhaustion had a 6.03-fold increased odds of placental abruption (aOR=6.03; 95% CI 2.38-15.32) as compared with the referent group (P-value for this additive interaction term=0.77). Inferences from these exploratory analyses, however, were limited by the small sample size.

DISCUSSION

Women who reported short (≤ 6 hours) or long (≥ 9 hours) sleep duration, during early pregnancy had higher odds of abruption when compared with women who slept 7-8 hours per night. Additionally, maternal complaint of vital exhaustion was associated with an increased risk of abruption, independent of sleep duration. To the best of our knowledge, this is the first study examining associations of sleep duration and vital exhaustion with abruption risk.

Despite awareness of pregnancy associated metabolic and morphological changes that contribute to poor and fragmented sleep during pregnancy [13-14], little has been done to properly and comprehensively assess the influence of disturbed sleep on perinatal and maternal health. Appallingly little is known about the impact of maternal sleep during pregnancy on perinatal outcomes. Insomnia, sleep disordered breathing (snoring or diagnosed obstructed sleep apnea) and restless leg syndrome are noted common complaints of pregnant women [14-16]. Though prior studies of sleep and pregnancy have provided useful descriptive information concerning the prevalence of these sleep disorders [17], few have evaluated the contributions of short sleep duration to the incidence of obstetric complications. A number of studies have documented increased risks of gestational hypertension, preeclampsia, preterm delivery, and intrauterine growth restriction with maternal self-reported snoring during pregnancy [15, 18]. In their pilot study of 19 healthy pregnant women, Okun et al [11] noted that maternal self-reported short sleep duration and poor sleep efficiency in both mid and late pregnancy were associated with higher concentrations of IL-6, which are predictive of PTD. However, we are not aware of any study that has evaluated matenal sleep habits or disorders in relation to abruption risk. Overall, our findings are consistent with other studies reporting associations of maternal

sleep disorders and short sleep duration with adverse pregnancy outcomes including preterm birth, low birth weight, and preeclampsia [9-10, 19].

Limitations of the data

Several potential limitations should be taken into consideration when interpreting the results of our study. First, our analyses are based on a case-control design, which may be subject to recall bias. Future prospective studies that allow for assessing early pregnancy sleep traits prior to the onset of signs and symptoms of abruption will minimize the likelihood of bias. Second, maternal nightly sleep duration during early pregnancy was obtained from self-report, and thus is likely susceptible to misclassification. Reported sleep duration is known to be moderately correlated with wrist actigraph-measured sleep duration ($r = 0.47$), and reports are typically longer by about 34 minutes for each hour of objectively measured sleep [20]. Third, our analysis, which focused on maternal sleep and exhaustion status in early pregnancy, may have missed the acute influence of later pregnancy sleep habits and vital exhaustion. A recent case-crossover study by Hendandez-Diaz [21] suggests that acute sleep disturbances may indeed be a “trigger” of adverse perinatal outcomes (e.g., spontaneous preterm labor and preterm premature rupture of membranes). More studies are needed to specifically assess trimester-specific sleep characteristic with outcome, and additional case-crossover studies are need to assess the acute influences of risk putative perinatal risk factors . Fourth, we did not collect information on frequency and duration of naps taken by mothers in this study, thus total sleep duration may be underestimated. Future studies will require making objective assessments of maternal nightly sleep duration, number and duration of naps during the day, and sleep quality. Fifth, we did not have data concerning participants’ shift-work or insomnia status thus cannot attribute observed associations of short sleep duration with placental abruption to occupational or medical conditions associated with short sleep duration. Lastly, although we adjusted for multiple confounding factors, as with all observational studies, we cannot exclude the possibility of some residual confounding. For example, early pregnancy iron deficient anemia (IDA) is documented as a risk factor of abruption [22]. However, we did not have information on maternal early and mid-pregnancy IDA and so were not able to adjust for this potential confounding factor.

Some biological mechanisms may plausibly account for the observed associations of maternal sleep duration and abruption risk. Alterations in the hypothalamic-pituitary-adrenal (HPA) axis following sleep loss could be one possible mechanism. Changes in the HPA axis have been shown to increase blood pressure levels after partial sleep loss in experimental settings [23]. Similarly, investigators have documented that disruptions in nocturnal cortisol secretion acutely increases blood pressure associated with partial sleep loss [24-25]. These metabolic perturbations could trigger abruption. Moreover, the HPA system becomes highly sensitive to negative feedback inhibition as a result of partial sleep deprivation [26]. Increased secretion of catecholamines [23] abnormalities in sympathovagal balance [24] and abnormal secretion of vasoactive hormones such as endothelin, vasopressin, and aldosterone [27] have been some mechanisms thought to link acute and/or chronic sleep duration with vascular disorders including hypertensive disorders and possibly abruption.

Long sleep duration was also associated with elevated abruption risk. We speculate that unmeasured confounders may lead to both abruption and increased need for sleep. Sleep disordered breathing, for example, has been shown to be associated with hypertensive disorders [28] including preeclampsia [15], and is known to fragment sleep. Hence, an alternative hypothesis is that maternal conditions associated with mild chronic inflammation such as depression, insulin resistance, and obesity [29] may contribute to longer sleep times and alterations in sleep inducing pro-inflammatory cytokines, including interleukin-1 [30] and tumor necrosis factor-α [31]. Whatever the mechanisms, the positive relationship between maternal habitual short and long sleep duration with abruption was evident in our study. Taken together with previously published studies concerning sleep disorders and sleep duration in pregnancy, these results suggest important health benefits of improved sleep hygiene before and during early pregnancy. If confirmed by other studies, our findings may motivate increased efforts aimed at exploring lifestyle approaches, particularly improved sleep habits, to lower the risks of adverse pregnancy outcomes including placental abruption.

In summary, our results suggest that the risk of placental abruption is increased in pregnant women with short and long sleep durations in early pregnancy and among those who complain about exhaustion. Comprehensive efforts are required to carefully characterize reproductive sequelae of sleep deprivation and sleep disorders among reproductive aged and pregnant women. Longitudinal cohort studies, with objective assessments of sleep duration and sleep quality during pregnancy are needed to confirm our findings and to assess whether volitional short sleep duration and/or insomnia contribute to metabolic perturbations that lead to adverse pregnancy outcomes such as placental abruption. Potential public health efforts to screen and treat affected women may also modify risks of abruption and possibly other associated disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

The authors wish to thank the staff of the Hospital Nacional dos de Mayo, Instituto Especializado Materno Perinatal, Hospital Edgardo Rebagliati Martins, Hospital Nacional Hipolito Unanue, and Hospital Nacional Docente Madre Niño San Bartolomè, Lima, PERU for their technical assistance with this research. The authors also wish to thank the dedicated staff members of Asociacion Civil Proyectos en Salud (PROESA), Peru.

ROLE OF FUNDING SOURCE

This research was supported by awards from the National Institutes of Health (NIH), National Institute on Minority Health and Health Disparities (T37-MD001449), and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (R01-HD-059835; R01-HD-059827). The NIH had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

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Table 1

Socio-Demographic and Reproductive Characteristics and Infant Outcomes in the Study Population, Lima, Peru, 2009-2010

Characteristics	Placental Abruption				P-value
	Controls (n=160)		Cases (n=164)		
	n	%	n	%	
Maternal age at delivery (years)	27.6 ± 5.8*		28.2 ± 6.5*		0.37
<20	10	6.3	13	7.9	0.66
20-29	88	55.0	80	48.8	
30-34	36	22.5	38	23.2	
≥35	26	16.2	33	20.1	
Primiparity	75	46.9	74	45.1	0.75
≤High school education	111	69.4	112	68.3	0.83
Employed during pregnancy	63	39.4	63	38.4	0.86
Planned pregnancy	105	65.6	110	67.1	0.78
No prenatal care	8	5.0	24	14.6	0.004
No prenatal vitamin	30	18.8	36	22.0	0.47
Smoking during pregnancy	0	0.0	1	0.6	---
Alcohol use during pregnancy	61	38.1	51	31.1	0.18
Illicit drug use during pregnancy	0	0.0	4	2.4	---
Pre-pregnancy weight (kg)	57.5 ± 9.2*		57.6 ± 9.0*		0.90
Infant birthweight (grams)	3348 ± 463*		2404 ± 928*		<0.001
Low birthweight (<2500 g)	7	4.4	86	52.4	<0.001
Preterm delivery (<37 weeks)	1	0.6	86	52.4	<0.001
Hours of sleep per night	7.4 ± 1.2*		7.4 ± 1.5*		0.91
Ever complaint of vital exhaustion	90	56.3	123	75.0	<0.001

*Mean ± SD (SD: standard deviation)

Table 2

Odds Ratio and 95% CI of Placental Abruption According to Maternal Sleep Duration and Vital Exhaustion during the First Six Months of Pregnancy, Lima, Peru, 2009-2010

Exposure Parameters	Controls (n = 160)		Placental Abruption (n = 164)		Unadjusted		Adjusted *		Adjusted **	
					OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
	n	%	n	%						
Hours of Sleep per Night										
≤6 hours	23	14.4	36	22.0	1.90	1.06-3.43	2.01	1.09-3.69	1.89	1.01-3.56
7-8 hours	118	73.7	97	59.1	1.00	Referent	1.00	Referent	1.00	Referent
≥ 9 hours	19	11.9	31	18.9	1.98	1.06-3.73	2.11	1.09-4.09	2.18	1.10-4.29
Complaint of Vital Exhaustion										
Never	70	43.7	41	25.0	1.00	Referent	1.00	Referent	1.00	Referent
Ever	90	56.3	123	75.0	2.33	1.46-3.74	2.37	1.46-3.85	2.32	1.42-3.82
1-3 times/Month	*56*	*35.0*	*77*	*47.0*	*2.35*	*1.40-3.94*	*2.26*	*1.33-3.84*	*2.23*	*1.30-3.81*
4 time/Month - Weekly	*25*	*15.6*	*36*	*21.9*	*2.46*	*1.30-4.66*	*2.74*	*1.40-5.37*	*2.75*	*1.39-5.48*
Daily	*9*	*5.6*	*10*	*6.1*	*1.90*	*0.71-5.05*	*2.15*	*0.79-5.86*	*1.90*	*0.67-5.34*
P-value for linear trend						*0.002*		*0.001*		*0.001*

* Adjusted for maternal age (continuous), pre-pregnancy weight (continuous), prenatal care and alcohol consumption during pregnancy

** Adjusted for maternal age(continuous), pre-pregnancy weight (continuous), prenatal care, alcohol consumption during pregnancy, as well as sleep duration or vital exhaustion

Table 3

Odds Ratio and 95% CI of Placental Abruption for Joint Categories of Maternal Sleep Duration and Complaints of Vital Exhaustion during the First Six Months of Pregnancy, Lima, Peru, 2009-2010

Night Hours of Sleep & Exhaustion	Controls (n = 160)		Abruption (n = 164)		Unadjusted OR		Adjusted OR	
	n	%	n	%		(95% CI)		(95% CI)
7-8 hours & no exhaustion	54	33.8	25	15.2	1.00	Referent	1.00	Referent
≤ 6 hours & no exhaustion	6	3.7	7	4.3	2.52	0.77-8.28	2.80	0.82-9.58
≥ 9 hours & no exhaustion	10	6.2	9	5.5	1.94	0.70-5.38	1.93	0.69-5.38
7-8 hours & any exhaustion	64	40.0	72	43.9	2.43	1.36-4.35	2.56	1.40-4.67
≤ 6 hours & any exhaustion	17	10.6	29	17.7	3.68	1.72-7.91	4.02	1.82-8.88
≥ 9 hours &any exhaustion	9	6.3	22	13.4	5.28	2.13-13.10	6.03	2.38-15.32
Interaction P-value (short sleep & any exhaustion)					0.47		0.42	
Interaction P-value (long sleep & any exhaustion)					0.87		0.77	

*Adjusted for maternal age, pre-pregnancy weight, prenatal care and alcohol consumption during pregnancy