

Effect of pregnancy-specific stress on spontaneous preterm birth among Chinese people

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Summary

Background: The current evidence implicates that psychosocial stress, especially pregnancy-specific stress, is associated with the risk of spontaneous preterm birth. The aim of the present study was to determine the effect of pregnancy-specific stress on spontaneous preterm birth among Chinese people. **Materials and Methods:** A total of 2,189 pregnant women were enrolled and followed up until parturition from February 2011 to January 2012. Maternal pregnancy-specific stress was assessed using the revised Pregnancy Stress Rating Scale (PSRS) at third trimester in pregnancy. Socio-demographic and psychological data were collected through interviews, medical, and obstetrical examination records. **Results:** High levels of maternal pregnancy-specific stress during the third trimester increased risk of spontaneous preterm birth compared with the low and medium levels (adjusted risk ratios, 2.92; 95% confidence interval, 1.12 - 7.58). The first stressor from the revised PSRS includes a risk factor for the safety of infants. **Conclusions:** High level of pregnancy-specific stress in third trimester might predict spontaneous preterm birth.

Key words: Pregnancy-specific stress; Spontaneous preterm birth; Revised PSRS; Third trimester; Stressor; Effect of PEQ on SPB.

Introduction

According to reports, 9.6% of total births across the globe in 2005 were preterm birth that accounts for 85% in Africa and Asia [1]. Prevalence of preterm birth is similar in China, ranging from 5-15%. Preterm birth is a major contributor to neonatal morbidity and mortality in poor perinatal outcomes. Some long-term complications, particularly cardiovascular and metabolic diseases which affect premature infants, could persist in later adult life [2]. Preterm delivery becomes a significant perinatal health problem throughout the world [1], which leads to an important economic burden for the society and individual. Approximately 75% of preterm births are attributed to spontaneous preterm birth; its etiology is still however unknown.

Psychosocial stress has been observed to be responsible for preterm birth and a crucial risk factor for poor perinatal outcomes in recent years. Although the methodology to measure psychosocial stress have improved, it appears that the association between stress and adverse perinatal outcomes remains controversial. Stressors such as major life events, work stress, daily hassles, and neighborhood safety *et al.* were investigated by most studies, whereas pregnancy-specific stress as a potential risk factor for spontaneous preterm birth was less studied. Pregnancy-specific stress, defined as maternal fears and worries pertaining to pregnancy [3], was indicated as a reliable predictor of preterm

birth in recent years [4, 5]. Most studies paid attention to the influence of pregnancy-specific stress on preterm birth at a certain gestational period [4, 6], but few were interested in investigating the exposure time [3] and perceived impact originated from pregnancy-specific stress. Especially in China, it is scarcely regarded as a risk factor for preterm birth.

Coping was defined as “cognitive and behavioral efforts to manage demands perceived as taxing or exceeding one’s resources” [7]. Coping is a mediator, which pregnant women could use to help deal with psychological stress. As a buffer of stress, social support might have a positive effect on pregnant women. It can inspire and encourage pregnant women to take measures to alleviate psychological stress, alter bad lifestyles, and persist in regular antepartum care. It was been shown in few articles that preterm birth could occur when faced with the absence of partner support [8]. Nevertheless, most studies demonstrated that social support could decrease the incidence of preterm birth [9, 10].

Maternal psychosocial stress has been extensively examined; to the present authors’ knowledge, epidemiologic research remains inadequate in China. Hence this study was designed with the objective to investigate the effect of spontaneous pregnancy-specific stress on preterm birth in the third trimester.

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Materials and Methods

Study population

A prospective study was conducted in the First Affiliated Hospital of Sun Yat-sen University and Guangzhou Women and Children's Medical Center from March 2011 to March 2012 and 2,575 pregnant women in third trimester were enrolled to complete a self-designed questionnaire. A total of 2,189 valid questionnaires were received, 130 of 2,189 mothers delivered premature infants and comprised the case group and 2,059 with normal term pregnancy as the control group. The questionnaire was designed by reviewing literature and referred to relevant questionnaires. They were presented to the pregnant women who participated in the antenatal examination at the two hospitals. Written consent form and detailed information of the study were obtained from all the participants.

The questionnaire consisted of three parts. The first part included socio-demographic characteristics including maternal age, years of education, average monthly income, pre-pregnant body mass index (BMI), and so on. The second part included three scales, the Revised Pregnancy Stress Rating Scale (PSRS), Simplified Coping Style Questionnaire (SCSQ), and Social Support Scale. The last part included information on birth outcomes including gestational age, birth weight, and delivery mode, etc.

The exclusion criteria were as follows: in terms of previous documented impact of race on preterm birth, the present subjects were Han Chinese. The women that had miscarriage, stillbirth, abnormality, medically induced preterm, and previous history of poor pregnancy outcome (prior preterm birth, stillbirth) were excluded from the study. Age less than 20 years, not planning to deliver, and continuing prenatal care at the two hospitals were also ineligible. Mothers who became pregnant by assisted reproductive techniques were not included either. Other women were rejected for medical and obstetric-related complications (such as heart diseases, diabetes mellitus, immunological diseases, hypertensive disorder complicating pregnancy, multiple pregnancy, mental disease, and so forth).

To assess the particular contribution of pregnancy-specific on spontaneous preterm birth, it was considered vital to eliminate confounding factors. For this reason, sociodemographic and psychological factors reported to be linked to mother's stress and spontaneous preterm birth were controlled in the present research.

The revised PSRS

The modified inventory for the assessment of maternal pregnancy-specific stress was adapted from the 30-item PSRS and was designed in 1989 by Chen *et al.* and adapted with a slight modification for fitting mainland Chinese [11]. The revised PSRS was used to survey maternal exposure to the stressors experienced by gravid women during third trimester (28-36 weeks). The PSRS mainly consists of three structure factors which are stress from the identification of mother's role (Factor 1:15 items), stress of pregnancy and delivery (Factor 2:8 items), and stress of altered appearance (Factor 3:4 items) [11]. The pregnant women were required to respond to the items of the revised PSRS during the trimester. Furthermore, the stressful extent of the responders experienced was based on a four-point scale ranging from 0 to 3 representing no stress, minor stress, moderate, and serious stress, respectively. The total scores were divided with total items, and total value of self-perceived impact rating of 0, 0.001 - 1.000, 1.001 - 2.000, and 2.001 - 3.000 referring to no stress, low stress, medium stress, and high stress, respectively.

SCSQ

The Chinese Edition of SCSQ was developed by Xie in 1998 to evaluate coping style [12]. The instrument included 20 items on a four-point scale ranging from 0 (never) to 3 (always). The coping styles were sorted into two categories: positive coping (from 1 to 12

Table 1. — Characteristics of 2,189 participants according to spontaneous preterm birth.

Maternal characteristics	n (n=2189)	%	Preterm, %	RR	95% CI value	p
Maternal age, years						
20-24	235	10.7	6.0	0.56	0.25-1.22	0.144
25-29	1147	52.4	5.6	0.52	0.28-0.97	0.040
30-34	680	31.1	5.7	0.53	0.28-1.03	0.062
≥35	127	5.8	10.2	1.00		
Maternal education, years						
≤ 12	550	25.1	8.7	1.82	1.25-2.63	0.002
> 12	1,639	74.8	5.0	1.00		
Monthly household Income, Yuan						
≤ 3000	465	21.2	9.9	2.88	1.80-4.60	<0.001
3000 - 5000	881	40.3	6.0	1.68	1.07-2.64	0.026
> 5000	843	38.5	3.7	1.00		
Maternal pre-pregnant BMI*						
Underweight	550	25.1	6.9	0.78	0.36-1.66	0.511
Normal weight	1,536	70.2	5.4	0.60	0.29-1.22	0.159
Overweight or Obese	103	4.7	8.7	1.00		
Social support [†]						
Low	593	27.1	8.8	2.83	1.65-4.85	<0.001
Medium-low	440	20.1	5.7	1.78	0.97-3.27	0.065
Medium-high	577	26.4	5.9	1.85	1.04-3.28	0.036
High	579	26.5	3.3	1.00		
Coping style [‡]						
Low	521	23.8	9.4	1.92	1.19-3.09	0.007
Medium-low	619	28.3	4.7	0.91	0.53-1.54	0.722
Medium-high	484	22.1	4.8	0.92	0.53-1.62	0.777
High	565	25.8	5.1	1.00		

Note: CI: confidence interval; * BMI: body mass index; underweight: BMI < 18.5kg/m²; normal weight: BMI 18.5 - 24.9 kg/m²; overweight or obese: † BMI > 25 kg/m².

‡ Social support was disposed as quartiles and sorted into low, medium-low, medium-high, and high social support.

§ Coping style was disposed as quartiles and sorted into low, medium-low, medium-high, and high coping style.

items) and negative coping (from 13 to 20 items). The total scores were calculated by average dimension of positive and negative coping and sorted into low, medium-low, medium-high, and high coping by using quartiles, respectively. Higher scores represented a better coping style. Primary data showed that the SCSQ possessed an adequate reliability ($\alpha=0.89$) and a good internal consistency (Cronbach's $\alpha=0.78$) [12].

Social Support Scale

The Chinese Edition of Social Support Scale [13] was used to evaluate the degree of pregnant women who obtained support from family, friends, neighbors, and other people through living. The self-report scale consists of ten items (three item objective support, four item subjective support, and three item utilization of social support). The ten items were summed to acquire total scores ranging from 10 to 64 which were sorted into low, medium-low, medium-high, and high support by using quartiles, respectively. Higher scores represented a better social support.

Statistical analysis

Epidata 3.0 software was used to build database and questionnaire entry. The Statistical Package for Social Science (SPSS) ver-

Table 2. — Characteristics of 2,189 participants according to perceived impact of the revised Pregnancy Stress Rating Scale (PSRS) in third trimester.

Maternal characteristics	Perceived stress of PSRS				χ^2	<i>p</i>
	0 (n/%)	0.001-1.000 (n/%)	1.001-2.000 (n/%)	2.001-3.000 (n/%)		
Maternal age, years					7.79	0.57
20-24	17 (7.2)	182 (77.4)	28 (11.9)	8 (3.4)		
25-29	107 (9.3)	801 (69.8)	197 (17.2)	42 (3.7)		
30-34	56 (8.2)	488 (71.8)	110 (16.2)	26 (3.8)		
≥35	13 (10.2)	87 (68.5)	24 (18.9)	3 (2.4)		
Maternal education, years					3.26	0.35
≤12	49 (8.9)	405 (73.6)	77 (14.0)	19 (3.5)		
>12	144 (8.8)	1,153 (70.3)	282 (17.2)	60 (3.7)		
Monthly household income, Yuan					10.2	0.11
≤ 3000	48 (10.3)	319 (68.6)	77 (16.6)	21 (4.5)		
3000 - 5000	86 (9.8)	612 (69.5)	149 (16.9)	34 (3.9)		
> 5000	59 (7.0)	627 (74.4)	133 (15.8)	24 (2.8)		
Maternal pre-pregnant BMI*					3.05	0.80
Underweight	46 (8.4)	387 (70.4)	98 (17.8)	19 (3.5)		
Normal weight	137 (8.9)	1,098 (71.5)	247 (16.1)	54 (3.5)		
Overweight or Obese	10 (9.7)	73 (70.9)	14 (13.6)	6 (5.8)		
Social support [†]					4.69	0.86
Low	57 (9.6)	414 (69.8)	102 (17.2)	20 (3.4)		
Medium-low	38 (8.6)	323 (73.4)	61 (13.9)	18 (4.1)		
Medium-high	46 (8.0)	408 (70.7)	100 (17.3)	23 (4.0)		
High	52 (9.0)	413 (71.3)	96 (16.6)	18 (3.1)		
Coping style [‡]					7.43	0.59
Low	47 (9.0)	373 (71.6)	80 (15.4)	21 (4.0)		
Medium-low	52 (8.4)	447 (72.2)	106 (17.1)	14 (2.3)		
Medium-high	48 (9.9)	334 (69.0)	84 (17.4)	18 (3.7)		
High	46 (8.1)	404 (71.5)	89 (15.8)	26 (4.6)		

* BMI: body mass index; underweight: BMI < 18.5 kg/m²; normal weight: BMI 18.5 - 24.9 kg/m²; overweight or obese: BMI > 25 kg/m².

[†] Social support was disposed as quartiles and sorted into low, medium-low, medium-high, and high social support.

[‡] Coping style was disposed as quartiles and sorted into low, medium-low, medium-high, and high coping style.

sion 16.0 software was used to obtain descriptive statistics. Test-retest stability of the revised PSRS was evaluated using Pearson correlation. Quartiles statistics were performed to describe the coping style and social support scales. Crude risk ratios (RR) and 95% confidence intervals (CI) were performed to determine the relationship of covariates with spontaneous preterm birth by means of single-factor logistic regression analysis. Chi-square analysis was used to determine the correlation between covariates and pregnancy-specific stress. Unconditional multiple logistical regression was used to adjust the confounding factors and determine the correlation between pregnancy-specific stress and spontaneous preterm birth. The confounding factors included maternal education (≤ 12 years, >12 years), monthly household income (≤ 3000 Yuan/month, 3000 - 5000 yuan/month, > 5000 Yuan/month), pre-pregnant BMI (under weight: BMI < 18.5 kg/m², normal weight: BMI 18.5 - 24.9 kg/m², overweight or obese: BMI > 25 kg/m²), social support (low, medium-low, medium-high, high), and coping style (low, medium-low, medium-high, high). A *p* value of < 0.05 was considered as statistical significant in the present research.

Results

Table 1 shows the descriptive characteristics, RR, and 95% CIs for preterm birth. To summarize, the mean age of the respondents was 28.7 (SD±3.5) years, while 5.8% were more

than 35 years. In the study, 130 of 2,189 mothers delivered premature infants. Nearly 75% of the participants had completed senior high school. Almost one-fifth of mothers were reported to have a lower income (21.2%). A total of 1536 (70.2%) mothers had a BMI of 18.5 - 24.9 kg/m².

The results of single-factor logistic regression analysis showed that the participant age of 25-29 years was a protective factor for spontaneous preterm birth (RR = 0.52, 95% CI: 0.28-0.97, *p* = 0.04). Possible risk factors for spontaneous preterm birth: years of maternal education < 12 years (RR = 1.82, 95% CI: 1.25 - 2.63, *p* = 0.002), average monthly income less than 3,000 Yuan (RR = 2.88, 95% CI: 1.80 - 4.60, *p* < 0.001), low scores of social support (RR = 2.83, 95% CI: 1.65 - 4.85, *p* < 0.001) and low scores of coping style (RR = 1.92, 95% CI: 1.19 - 3.09, *p* = 0.007). Others factors were found to have obvious correlation with spontaneous preterm birth.

Table 2 shows different levels of perceived pregnancy-specific stress across demographic and psychosocial characteristics during third trimester. Pregnancy-specific stress had no correlation with socio-demographic characteristics and psychosocial factors.

Table 3. — Crude and adjusted RRs for perceived impact of the revised PSRS on spontaneous preterm birth in third trimester.

Perceived stress of PSRS	Preterm (n/%)	RR	Crude 95% CI	<i>p</i>	RR	Confounder adjustment 95% CI	<i>p</i>
0	9 (4.7)	1.00			1.00		
0.001 - 1.000	89 (5.7)	1.24	0.61 - 2.50	0.55	1.32	0.65 - 2.68	0.45
2.001 - 3.000	22 (6.1)	1.34	0.60 - 2.96	0.48	1.43	0.64 - 3.19	0.39
2.001 - 3.000	10 (12.7)	2.96	1.16 - 7.60	0.02	2.92	1.12 - 7.58	0.03

CI: confidence interval.

The relationship between pregnancy-specific stress and spontaneous preterm birth during third trimesters with unadjusted and adjusted confounding factors are presented in Table 3. The results of multi-factors logistic regression analysis showed that participants with high level of pregnancy-specific stress were susceptible to spontaneous preterm birth in third trimester when compared with the low and medium levels (RR = 2.96, 95% CI: 1.16 - 7.60, $p = 0.02$) and the low and medium categories presented no associations with spontaneous preterm birth. Although the risk ratios of spontaneous preterm birth associated with high level of pregnancy-specific stress in third trimester slightly decreased from 2.96 to 2.92, the relationship between them remained significant after adjusting possible confounding factors such as maternal years of education, average monthly income, pre-pregnant BMI, social support, and coping style (adjusted RR = 2.92, 95% CI: 1.12 - 7.58, $p = 0.03$). After adjusting confounding factors, the risk ratios of spontaneous preterm birth associated with low and medium levels of pregnancy-specific stress slightly increased without significant differences. In contrast to participants with low and medium levels of pregnancy-specific stress, women with high-level stress had more than two-fold greater risks of spontaneous preterm birth.

Discussion

According to the findings of the study, a relevance of pregnancy-specific stress and spontaneous preterm birth by using perceived impacts during third trimesters was presented. The research indicated that prenatal maternal exposure to higher levels of stress originated from pregnancy-specific stress was associated with the increasing risk of spontaneous preterm birth during pregnancy. The finding was an extension of previous studies [14, 15]. It was implicated that pregnancy-specific stress in the third trimester had an association with spontaneous preterm birth. At present, many studies accumulated on examining the association between pregnancy-specific stress and spontaneous preterm birth in the second trimester. Dole *et al.* [6] declared that mothers with high counts of pregnancy-related anxiety had a high risk of preterm birth in

mid-pregnancy. The study conducted by Orr *et al.* [4] found that pregnancy-related anxiety contributed to spontaneous preterm birth at mean of 16 weeks of gestation. Few articles paid attention to the occurring of pregnancy-specific stress during the time windows for preterm birth. Roesch *et al.* [16] examined the effect of state anxiety, pregnancy-specific anxiety, and perceived stress on gestational length at three time points during pregnancy. Their results showed pregnancy-specific anxiety was related to shorter gestation. Similarly, the impact of a series of stressors on several birth outcomes during three trimesters in pregnancy was investigated by Lobel *et al.* [17]. They found that pregnancy-specific stress directly predicted preterm birth. The present findings were partially consistent with the studies.

The reasons for the inconsistent results might be as follows. First of all, the mechanisms that underlay the relationship between stress and preterm birth remained plausible and unclear. It was considered that hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system played a vital role in stress procession. The exposure time is crucial to the influence of maternal stress on preterm birth. Hobel *et al.* [18] proposed the increased cortisol might lead to placental, suppress fetal pituitary, and inhibit fetal growth when mothers had high levels of stress in the first trimester. Mancuso *et al.* [19] found that women with high corticotropin-releasing hormone (CRH) levels and high stress at 28 to 30 weeks gestation had shorter gestational age, which might predict preterm birth in mid-pregnancy. The study of Obel *et al.* [20] showed psychological stress in late pregnancy was related to high levels of cortisol. It was hypothesized that maternal HPA axis might contribute to preterm birth through the association with fetal placental unit. Maternal stress caused the release of cortisol, CRH, epinephrine, and norepinephrine which increased placental CRH concentrations. In turn, placental CRH further stimulated the release of the aforementioned hormones [18] and mediated the fetal stress response [21]. Inflammation, immune reaction, and vascular disorder were involved in stress processes [22]. Finally the factors interacted and might initiate parturition.

Secondly, examination of stress processes during pregnancy was sophisticated by the influence of maternal demographic and socioeconomic characteristics and mother's behaviors. As it is well known, maternal age, education, economic status, and race *et al.* all might be risk factors for preterm birth across maternal stress. Stress might affect maternal behaviors including smoking, eating, and sleeping. Maternal poor behaviors such as cigarette smoking and substance use were indicated in preterm birth [23].

Thirdly, the inconsistent results partly derived from defining and measuring stress. Regarding conceptual and methodological discrepancy, it is not simple to ascertain what type of stress might trigger preterm birth and during which trimester of pregnancy. Usually, the effects of all kinds of stress (such as life events stress, chronic stress,

perceived stress, daily hassles, pregnancy-specific anxiety, *et al.*) on birth outcomes were investigated [24]. Thus the study on stress and preterm birth remains difficult to assess in multiple factors.

In the current research, social support and coping styles were examined as confounder factors. The present data implicated that low levels of social support and coping style might predict preterm birth. However, they did not change the relationship between pregnancy-specific stress and spontaneous preterm birth. Norbeck and Tilden [25] formulated the "buffer hypothesis" in which the social support might buffer the influence of stress on birth outcomes in pregnancy. However, the buffer evidence was lacking and most studies implicated that support hardly mediated the stress and preterm birth. Several studies indicated social support might act as moderator between stress and birth outcomes [6, 26], whereas others showed that social support did not change the effects of stress on birth outcomes such as preterm birth and gestational age [9, 27]. The present result was consistent with the latter.

Previous research involving the coping strategy, stress, and adverse birth outcomes remains inconsistent [23, 28]. Two studies implicated poor coping style increased preterm birth risk [29, 30]. In contrast, the present findings indicated coping style did not modify the relationship between stress and preterm birth. There might be two reasons for the inconsistent results: the first one is that social support and coping style might play buffer or moderator role in mediating the effects of stress on birth outcomes and the second one is that racial, cultural, and ethnic factors might influence social support and coping processes. Social support and coping style are associated with maternal characteristics such as personality.

However, the limitations of the present study should be noted. Firstly, the authors only examined one multiple psychological stressor without others, such as chronic stress, daily hassles, state-trait anxiety, etc. Moreover, physiological indicators of stress such as CRH and cortisol, etc., were not examined. The evidence that stress hormones interacted with psychological stress remained deficient. Further studies should investigate the association between stress and physiological markers of stress and find a biologic pathway through what kinds of stress cause poor birth outcomes. Secondly, a crucial measurement issue is worthy of consideration. According to the strata by perceived impact weighting of stress, pregnant women at a certain stress level comprised a very small proportion, leading to limited convincing evidence. Thirdly, the revised PSRS was scarcely employed to evaluate the relationship to preterm birth in China. Further research is required to explore the factor structure of the revised PSRS. Lastly, although this was a prospective based study, stress was measured at the end of third trimester retrospectively. Hence, recall bias was still inevitable. Despite the limitations, the methodological strengths of the present research includes prospective de-

sign, controls for possible risk factors, and assesses stressors by rating perceived impact rather than counts.

In conclusion, the evidence of association between psychosocial stress and preterm birth was confirmed in the present study. Moreover, it is suggested that third trimester-specific exposure may play a crucial role in the relationship between psychosocial stress and preterm birth. In addition, an approach as intervention to decrease spontaneous preterm birth risk was provided. Future studies should be carried out to examine more stressors and explore possible biologic pathway during pregnancy.

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