

Maternal stress and preterm delivery

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Research on stress and birth outcomes originated approximately 25 years ago¹ with the earliest published empirical studies on the role of stress in preterm delivery appearing in the 1970s^{2,3}. Over time, nearly three dozen studies have been published and approximately one dozen reviews summarize the results of research on the role of stress in preterm delivery^{4,5}. Prospective studies with larger samples, appropriate controls and standardized measures of stress are now available, providing a basis upon which to conclude that stress is a significant risk factor for preterm delivery⁶⁻⁸. Studies on preterm delivery and stress have been conducted in the United States and many other countries, and samples have included poor and ethnic minority women in order to understand stress in these sociodemographically at-risk groups. Results of this research suggest that the stress-preterm association appears to apply to women of many different nationalities, cultures and social classes with few exceptions⁹.

KEY FEATURES FOR STRESS-PRETERM RESEARCH

Most of the published studies in this area examine preterm delivery (< 37 weeks) as the outcome of interest, and a few examine gestational length (in weeks or days). Other studies examine preterm delivery in conjunction with low birth weight. Stress appears to have a linear association with gestational length, to predict preterm delivery, and to have independent effects on fetal growth restriction.

Research on stress and birth outcomes has examined several forms of stress using standardized or *ad hoc* scales administered in questionnaires or interviews. The most popular measures are those assessing major life events¹⁰, and those assessing anxiety,

especially state and trait anxiety¹¹. Recent research has examined other emotional states including depression and generalized distress^{12,13}. Research on work and household strain is also pertinent^{14,15}. As yet there has been little consideration of how these different stress concepts and measures compare in the prediction of preterm delivery. Comparison would enable practitioners to use stress measures more effectively in targeting women at risk, and facilitate the development of etiological models.

Published studies are quite uneven in their assessment of maternal demographics and of current and past medical conditions that may be confounded with stress⁴. These factors are sometimes treated as eligibility or exclusion factors in sampling, but otherwise must be controlled in multivariate analyses. It is necessary to control for age, socioeconomic status (e.g. income, education), marital status, ethnicity or race, parity and a host of medical risk factors, because younger, poor, unmarried and ethnic minority women experience greater stress in pregnancy in general, as do women having a first birth. Similarly, women at high risk due to complications in the current or past pregnancies, or because of general health problems such as heart or lung disease, may experience stress in pregnancy as a result of these risk conditions. Thus, all factors that cause stress and are known to pose risk for adverse outcome must be controlled in stress research. Until recently, studies have either lacked sufficient controls or been controlled for only some of these factors.

Finally, prospective studies have rarely included more than one assessment during pregnancy; those that do almost never study early pregnancy. Thus, evidence to date is based mainly on assessments of stress in the second trimester and is inconclusive as to when in pregnancy stress poses the greatest risk for

preterm labor and delivery. This issue is a key to determining when to intervene.

UCLA STRESS IN PREGNANCY STUDIES

Our program of research originated in 1984 and has involved five prospective longitudinal investigations concerning the role of stress in pregnancy with more than 3000 women. These investigations test not only the prediction of preterm delivery and gestational length, but also the prediction of low birth weight (adjusted for gestational length). Other psychosocial factors such as social support, personality, mastery, work strain and attitudes toward the pregnancy are also examined^{16,17}. Stress has been measured in comprehensive ways including detailed, standardized assessments of life events, anxiety, perceived stress and other stress-related concepts such as depression and work strain. Our samples reflect the demographics of the local communities in Los Angeles and Orange counties in the state of California; three studies sampled large groups of Hispanic women, including newer immigrants and less acculturated women interviewed in Spanish with carefully translated instruments. Two studies sampled large numbers of African-American women. Most of our samples have been of lower income and education. All studies included postpartum maternal assessments and one included infant assessments. We have also collected considerable information on fetal growth (by means of repeated ultrasounds), on neuroendocrine mediators such as catecholamines and corticosteroids, and on behavioral factors such as substance use, prenatal care, and nutrition assessed with a variety of methods. In sum, these studies provide unique information about the role of stress in preterm delivery.

UCLA STRESS IN PREGNANCY RESEARCH PROGRAM FINDINGS

Our first study of 130 pregnant women involved repeated assessments of stress using multiple measures collected throughout pregnancy, extensive coding of medical risk factors, and use of innovative multivariate techniques (structural equation modelling) to formulate a latent stress factor and simultaneously to test several hypotheses¹⁸. Results indicated that psychoso-

cial distress (a latent stress factor composed of state anxiety, perceived stress and life event distress) predicted gestational length, controlling for birth weight, medical risk, substance use and parity¹⁹. The composite stress variable in this study appears to reflect chronic stress, a form of stress now implicated in adverse health effects²⁰. In addition to a significant effect of stress on gestational age after controls, we found a marginally significant interaction of stress and medical risk, indicating that the negative association of stress and gestational age was most pronounced in women of high medical risk. The frequency of preterm deliveries was 17% in women with high stress and high medical risk whereas it was 6–9% with either high medical risk or high stress, and 3% in women with neither risk factor.

The primary goal of our second study was to examine stress and other factors as mediators of higher rates of low birth weight in ethnic minority groups giving birth for the first time^{21,22}. Over 1100 women were sampled, approximately two-thirds Mexican-Americans and Mexican immigrants, and one-third African-American. Only low-income women were eligible to participate as defined by strict objective criteria. Again, a composite stress variable combining life events, anxiety and perceived stress was computed. This study afforded an excellent opportunity to replicate the stress findings from our first study. Results indicated that women of high stress were 4.12 times at risk for preterm delivery ($p < 0.001$) controlling for medical risk factors, parity and substance use.

Our next three investigations were similar to the first two in using a variety of stress measures and coding medical risk factors carefully, but these studies included a wider range of income and education levels. One was a smaller study of 90 relatively affluent, English-speaking, non-Hispanic White women^{23,24}. Another study sampled approximately 250 women, half Hispanic and half White of low to middle socioeconomic status²⁵. The last was a large study of approximately 650 women of three ethnic groups (Black, White, Hispanic) and a range of socioeconomic status in each group²⁶.

Surprisingly convergent results were obtained in these three studies. In all three, the strongest predictor of gestational length and preterm delivery of all the

stress concepts was a new variable, *pregnancy anxiety*. This concept refers to items designed to assess fear and worries about the pregnancy itself, such as concern about how the baby is developing, of losing the baby, and of personal harm during delivery, and also questions on concern about having a difficult labor. When combined into a Pregnancy Anxiety index, these items significantly predicted gestational age, after controlling for medical risk and several other variables^{23,27}.

In the largest of the three studies, we had a simpler measure of pregnancy anxiety developed in order to administer it at each of three times in pregnancy (18, 28 and 36 weeks). Four adjectives (anxious, concerned, afraid, panicky) were rated to indicate how often a woman had felt these emotions *about being pregnant* in the past week. This four-item index predicted gestational age and preterm delivery, after controlling for age, education, income, marital status, parity and medical risk in a sample of over 500 women. The adjusted odds ratio was 1.54 ($p < 0.05$) indicating that women with high pregnancy anxiety were at 1.5 times higher risk of a spontaneous preterm delivery compared to women with lower pregnancy anxiety. State anxiety, perceived stress and life events were not as strongly predictive of outcomes. Tests of the associations of pregnancy anxiety at each of the three time-points in pregnancy to gestation length revealed that no single time-point was a better predictor.

MECHANISM OF STRESS-PRETERM ASSOCIATION

As the issue of whether psychosocial stress is a risk factor for preterm delivery becomes resolved and the nature of the stress responsible is clarified, further attention should be turned to the mechanisms or pathways by which stress contributes to preterm labor and delivery. Multiple mediating and interactive processes are likely to be involved including endocrine, immune and behavioral processes⁵. Past research on stress and catecholamines has been invoked as one explanation for how stress can contribute to the onset of labor²⁸. Newer work suggests a key role for stress hormones, especially corticotropin-releasing hormone (CRH), as one mediator of the stress-

preterm relationship^{29,30}. Precipitous rises in CRH appear to be precursors of early labor and may be contributed to by high levels of psychosocial stress. Converging evidence from our preliminary studies indicates that abnormally high levels of CRH in second trimester or even earlier may be useful in identifying women at risk for preterm labor^{25,31}.

Another possibility is that stress increases risky sexual behavior, decreases prenatal care utilization for the detection of infection, and lowers compliance with treatment thereby contributing to preterm deliveries associated with infection. Stress has also been associated with behaviors such as poor eating habits, smoking and substance use that increase risk for intrauterine growth retardation as a precipitator of early labor³². Finally, research suggests that women with lives characterized by high chronic stress tend to receive less social support. Stress may be a notable risk factor only when it occurs in the absence of network support or support services, thus creating a more general psychosocial vulnerability risk factor. These and other mechanisms are worthy of attention in future.

IMPLICATIONS AND CONCLUSIONS

In summary, pregnancy anxiety appears to be a component of general stress measures responsible for associations with gestational length and preterm delivery, and a single assessment in second trimester may be sufficient to detect this risk. By isolating this risk factor specifically, we may be better able to address issues of prediction, identification and risk reduction more precisely in future.

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