Association Between Life Stress and Serious Perinatal Complications

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The association between stressful life changes, social supports, and serious complications of pregnancy was measured in 513 women obtaining prenatal care in four rural family practices. Those women whose life change score (LCS) increased from the second to the third trimester had a significantly higher rate of poor outcomes (neonatal death, transfer to a neonatal intensive care unit, birthweight less than 2500 g or 5-minute Apgar score less than 7) than those whose LCS did not increase (9.2% vs 3.9%, P = .015). This effect of increasing stress was present even after controlling for demographic and standard obstetric risk factors. High life change scores at 20 weeks' gestation and 34 weeks' gestation were not individually associated with poor outcomes. Those with low social support did not have a statistically significant higher rate of complications, and social support did not buffer the adverse effects of increasing stress. This study shows that serious and clinically important complications of pregnancy are related to stressful life change independent of biomedical risk.

Several psychosocial factors have been associated with the outcome of pregnancy. Associations with adverse outcomes have been found for anxiety,[1–5] life stress,[5–10] low social support,[8–12] and family dysfunction.[11] Although there is general consensus that these factors influence the complication rate in pregnancy in some manner, many specific issues remain unresolved.

Several studies have demonstrated an effect of stress or social support on pregnancy outcome, but have used such broadly inclusive definitions of pregnancy complications[5,8–10] that outcomes as diverse as threatened abortion and prolonged labor and as unimportant as nuchal cord have been used to define the complicated pregnancy groups. In these studies, rates of complicated pregnancy reach nearly 50%. Such criteria call into question the clinical significance of the findings and defy any attempt to explain the biological basis of the effect of stress or social support.

Other studies have been differently limited by methodologic constraints. Some research has relied on measures of prenatal stress taken at the time of hospitalization for delivery.[4,7] It seems likely that recall bias would affect responses to such retrospective reports. Other studies have systematically excluded patients with high biomedical risk, have enrolled convenience samples of women presenting to large tertiary care centers, or have been hampered by small sample sizes. Still others have measured life changes (stress), a dynamic variable, at only one point in pregnancy.

Independent of methodologic issues, several credible studies have failed to demonstrate a link between poor outcome and psychosocial risk. Studies that have controlled for biomedical risk by excluding complicated patients or by using multivariate analysis have shown no relationship between pregnancy complications and anxiety, personality characteristics, social support, attitudes, or life stress.[13–15]

This current study prospectively measured the effect of stressful life change and social support on serious and important perinatal complications in a large group of pregnant, rural women and controlled for the potential confounding effect of biomedical risk.

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METHODS

Subjects and Sites

The study population was composed of pregnant women residing in four rural Missouri counties who came for prenatal care to one of four family practices involved in a research consortium.[16] The four practices are located in towns of 3000 to 10,000 persons; two are family medicine residency training sites. During a 2-year period from 1984 to 1986, pregnant women between 18 and 22 weeks' gestation were asked by physicians or office staff to participate in the project. They were told that this study was to help determine factors that might influence the outcome of pregnancy. Presentation at a gestational age greater than 22 weeks was the only prospective exclusion criterion; a decision was made to exclude late registrants because they could not complete the second trimester questionnaire during the 18- to 22-week gestation period. Pregnancies that ended prematurely before the 32- to 36-week gestation visit also were excluded from this study because data would not be available from both the second and third trimester visits.

Instruments

The questionnaire used to gather data about life stress was a 39-item adaptation of the Social Readjustment Rating Scale of Holmes and Rahe.[17] Slight changes in wording were made to account for pregnancy, and questions that were inappropriate for a pregnant subject were deleted. This scale was chosen because it has been used in numerous studies of stress and health effects. Each of the questionnaire items has a designated weight. For example, 100 points is assigned to the death of a spouse, 45 points for loss of a job, 20 points for a move, etc. Responses are summed to create a total life change score. The patients were asked to answer the questions to account for life changes occurring in the 12-month period preceding the visit.

Social supports were assessed as a summary score of six components of support derived from a 12-item questionnaire: personal networks, community networks, intimacy, appreciation–understanding, satisfaction–loneliness, and tangible assistance. The conceptual background for these measures of social support was articulated by Berkman and Syme[18] and Henderson et al.[19] Social support, as measured by this technique, has been found by McKay et al[20] to buffer the adverse effect of life stress on health.

The physician performing the delivery completed an outcome questionnaire. Standard perinatal outcome variables were used, and because adverse outcomes were relatively rare, a composite of perinatal complications was developed. A poor outcome was prospectively defined as the presence of at least one of the following: neonatal death, transfer of the infant to a neonatal intensive care unit, Apgar score of <7 at 5 minutes, or low birthweight (less than 2500 g). These outcomes were chosen because they are clinically important, easily measured, and definite, and because they can also be predicted by the biomedical risk index used in this study, thus allowing a procedure for controlling for biomedical risk.

Biomedical risk was assessed using an obstetric risk index developed by Coopland et al.[21] Coopland's index includes a series of standard, weighted prenatal risk factors that are summed to create a total risk score. This index was chosen from a variety of other validated indices because it used no intrapartum measures and because subjects in this study who scored highly on the Coopland index had a high rate of adverse outcomes. It was thus useful as a measure to control for biomedical risk. In a recent review of several risk indices, Coopland's index was found to have the highest sensitivity and specificity for perinatal mortality and depressed Apgar score.[22] Goodwin's index, which was slightly modified to form Coopland's index, was recently found superior to the indices of Hobel and Halliday[23] in a family practice setting.

Procedure

Because life change was conceived to be a dynamic variable, it was measured at two points in pregnancy. Pregnant patients were asked to complete demographic and stress and social support questionnaires during an office visit between 18 and 22 weeks' gestation and again between 32 to 36 weeks' gestation. Information about standard obstetric risk factors was collected at the same visits. These two periods were selected because they were late enough to avoid dropout from first trimester abortions and early enough to provide a measure of high risk when referral is still possible. Outcome data collection was completed by the delivering physician as soon as possible following delivery. When an infant or mother was transferred or referred to a specialist or intensive care unit, records regarding outcome were obtained from the receiving physician or institution.

Data Analysis

Life change was analyzed in three ways. First, the total life change score (LCS) from the 18- to 22-weeks' gestation visit was calculated and labeled LCS1. The one half of the group scoring above the median was the high-scoring group. Second, total life change score was calculated from the 32- to 36-weeks' gestation visit and labeled LCS2. Again, those scoring above the median were labeled the

TABLE 1. CHARACTERISTICS OF STUDY SAMPLE VS COUNTY POPULATION GIVING BIRTH IN 1985

Characteristic	Study Sample (%)	*County Population (%)
White race	94.2	97.2
Married	87.0	85.9
Education		
<12 years	19.5	22.3
Age (years)		
<20	14.0	13.8
20–34	83.2	80.8
>35	2.8	5.4
Cigarette smoker	26.5	30.3
Nulliparous	39.1	40.0
Birthweight <2500 g	1.8	5.9
Apgar score <8	5.3	4.3

From Missouri Vital Statistics 1985. Jefferson City, Mo, Department of Health, 1986.

TABLE 2. THREE MEASURES OF STRESSFUL LIFE EVENTS RELATED TO POOR OUTCOMES

Measure of Stressful Life Events	Proportion with Poor Outcome No. (%)	P
LCS1*		
High	16/257 (6.2)	.86
Low	15/256 (5.9)	
LCS2		
High	13/257 (5.1)	.35
Low	18/256 (7.0)	
Change in stress		
Increase	19/208 (9.1)	.015
No increase	12/305 (3.9)	

LCS1 denotes life change score at 18 to 22 weeks; LCS2 denotes life change score at 32 to 36 weeks. Change in stress is equal to LCS2 – LCS1. Differences compared using chi-square.

high-scoring group. Third, a change in stress level was calculated. Life change during the pregnancy rather than preceding it was postulated to have the most powerful impact on pregnancy outcome; therefore, a decision was made in advance to calculate a change in stressful life events score by subtracting the LCS1 from LCS2. This procedure provided a stressful event score quite specific to the time of pregnancy under study. Those women whose LCS increased were assigned to a group defined as experiencing increasing stress and those whose LCS did not increase were assigned to a group defined as not experiencing increasing stress.

Social support status was determined for the 32- to 36-weeks' gestation visit by combining the six social support categories and then creating two groups. Each subject was classified as having high (1) or low (0) support in each of the six social support categories. Social support was quantified by summing points from the categories, thus creating a scale ranging from 0 to 6. This scale was dichotomized to create a low social support group (about one third of the subjects) and a high social support group (about two thirds of the subjects).

Life change scores (high vs low) and social support (high vs low) were related to outcome (poor, not poor) using chi-square statistics. Analysis of possible confounding was done by using logistic regression to control for biomedical risk, education status, marital status, and race.

A contingency table relating outcomes for the cross product of high and low stress and high and low social support was created to ascertain whether there was a buffering effect of high social support on the adverse effects of high stress.

RESULTS

Complete life change, social support, and outcome data were available for 513 of the 646 subjects enrolled. Demographic and obstetric data characterizing the sample of subjects are presented in Table 1. In addition, these characteristics are presented for women living in the four counties represented and giving birth during the middle of the study period. The study sample is similar to the county population except for the percentage of low birthweight infants. The study excluded women giving birth prior to the 32- to 36-weeks' gestation visit, eliminating many premature infants from consideration. This methodologic decision almost certainly accounts for part of the discrepancy. In addition, some high-risk women may have bypassed the local system of care to be cared for in regional centers.

Thirty-one of the 513 pregnancies (6%) had one or more poor outcomes. There were three neonatal deaths, nine other infants were of low birthweight (less than 2500 g), and 10 more had 5-minute Apgar scores of less than 7. In addition, nine infants were transferred to a neonatal intensive care unit. The majority of infants with low Apgar scores and of low birthweight were also transferred to a neonatal intensive care unit.

Outcomes for the three methods of determining levels of stressful life change are listed in Table 2. A high LCS at

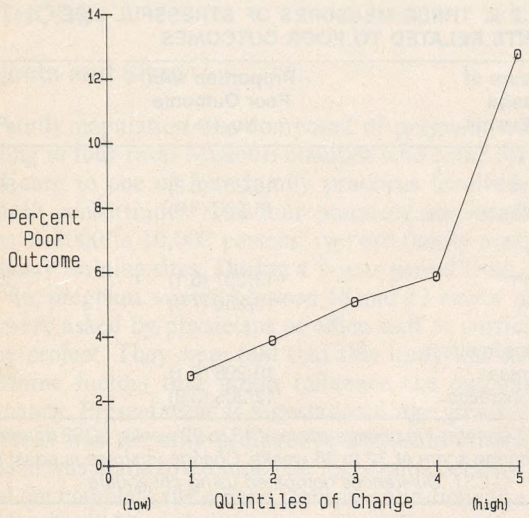

Figure 1. Magnitude of changes in life events and adverse outcome

TABLE 3. SOCIAL SUPPORT SCORES AT 32 TO 36 WEEKS' GESTATION AND OUTCOME

Social Support Score	Proportion with Poor Outcome No. (%)	P
Low	15/178 (8.4)	.17
High	16/335 (4.8)	
Total	31/513 (6)	

Low social support is lowest third; high social support is highest two thirds. Proportions compared with chi-square.

the 18- to 22-weeks' gestation visit was not associated with a significant increase in complications. Likewise, high scores at 32 to 36 weeks' gestation were not associated with a statistically significantly higher rate of poor outcome (5.1% vs 7.9%, $P = .35$). Those 208 women whose scores increased from the second to the third trimester, however, had a significantly higher rate of poor outcomes (9.1% vs 3.9%, $P = .015$) than the 305 women whose LCS did not increase. Figure 1 shows that the rates of poor outcomes increased for each quintile of life event changes and that there is a threshold effect between the fourth and fifth quintiles.

A comparison of high and low social support scores as they were associated with poor outcome is displayed in Table 3. Those women with a low social support score at 32 to 36 weeks' gestation had a higher rate of complicated pregnancy, but the difference was not statistically significant (8.4% vs 4.8%, $P = .17$).

Any interaction between life change and social support is shown in Table 4. Social support did not appear to buffer stress; a high incidence of poor outcomes was present in the subjects reporting increasing stress regardless of whether social support status was high (8.2%) or low (9.3%). The group with neither increasing life change nor low social support, however, had a much lower rate of poor outcome (2.2%) than did the groups with increasing life change, low social support, or both.

To ascertain whether biomedical risk factors confounded the relationship between stressful life change and outcome, a logistic regression was performed. Table 5 shows that increasing life change (high stress) was related to poor outcome even after controlling for biomedical risk using Coopland's scoring system ($P = .041$; odds ratio 2.7, 95% confidence limits 1.2 to 6.2). The addition of marital status, education level, and race to the model did not alter the findings regarding stressful life change.

DISCUSSION

In this cohort of patients, an increase in stressful life events during pregnancy was associated with a 2.3 times higher incidence of adverse outcome. High life change scores at 20 and 34 weeks' gestation were not associated with adverse outcomes. Hence, a one-time finding of high stress was not a predictor of poor outcome, but a progressive increase in stressful life change was associated with adverse outcome. The effect of stress was still present after controlling for the influence of biomedical risk factors. Social support, as measured in this study, did not by itself predict outcome in a statistically significant fashion, nor did it appear to buffer stress.

Previous research relating psychosocial factors to pregnancy outcome has yielded conflicting results, but in general this past work supports the contention that stressful life events influence the rate of complications of pregnancy. This study, with a large sample of rural women, confirms the adverse influence of stressful life change on pregnancy outcome. Some aspects of the present study are unique. First, the effect of stress was shown to be independent of biomedical risk by logistic regression. Second, this study used only clinically important perinatal morbidity as criteria in defining poor outcome.

The measure of life change used here, that of increasing stable or decreasing life change, is also unique. Although the method of subtracting one score from another is simplistic, it does take into account the important fact that life change (stress) is not stable. Women with consistently high life change scores, for example, may be able to adapt

TABLE 4. INTERACTION BETWEEN STRESSFUL LIFE CHANGE, SOCIAL SUPPORT, AND OUTCOME

Social Support	Stress: Not Increasing No. (%)	Stress: Increasing No. (%)
High	4/178 (2.2)	12/147 (8.2)
Low	7/92 (7.6)	8/86 (9.3)

Note: Proportions are number of poor outcomes over total subjects in cell with percentage of poor outcome per cell in parentheses.

TABLE 5. INCREASE IN PROBABILITY OF ADVERSE PERINATAL OUTCOME BASED ON MULTIVARIATE LOGISTIC REGRESSION MODEL

Variable	Odds Ratio	95% Confidence Limits
Coopland's risk score	1.3*	1.1, 1.6
Marital status	1.0	0.3, 3.7
Education	1.4	0.5, 3.5
Race	.6	0.1, 5.6
Stress	2.7	1.2, 6.2

**Odds ratio for each increment of 1 point in risk score.*

emotionally and physically to the changes. A woman with very few baseline life changes, when confronted with even modest levels of change, may well have more difficulty in adapting to the increase. This concept has not been previously explored and may prove helpful to other areas of stress research.

Social support, as it was measured in this cohort of pregnant women, did not buffer the effect of increasing life changes. There are alternative conceptual models to the buffer hypothesis, including independent effects and interactive effects with life change.[24] In the current study, 178 patients (35%) had neither high life changes nor low social support. The complication rate in this group was only 2.2% (Table 4). Hence, the absence of increasing stress and social isolation defined a sizable subset of patients at very low risk.

Some limitations should be considered when interpreting these data. All patients in this study were cared for by rural family physicians; most patients were white and had relatively low biomedical risk. The findings of this study may or may not be present in a high-risk or urban population. Because the study protocol necessitated measurements at specific times both in the second and third trimesters, women who presented for care after 22 weeks' gestation and who delivered before a visit at 32 to 36 weeks' gestation were excluded. This procedure excluded 11 patients who gave birth to low birthweight infants. It is possible that the experience of these women, with respect to social support and its association with outcome, may be different from the experience of those who delivered after 32 weeks. These data therefore cannot be applied to extremely premature infants. In addition, there were 122 other women who did not complete all items on both sets of the stress and social support questionnaires. Sociodemographic characteristics, outcome measures, and mean scores on the Coopland index did not differ between these 122 women and the 513 who were included in the study. These factors do not affect the primary conclusion that stress influences the outcome of pregnancy.

A major advantage of this study is its prospective design; stress and social support were measured before the outcome events. It is possible that the association between life stress and outcome was confounded by an intermediary, such as preeclampsia or diabetes, which could produce both stressful change and poor outcome. This possibility is very unlikely, however, because the effect of stress was independent of biomedical risk; Coopland's index includes these potential confounders.

Unfortunately, no unifying hypothesis links adverse life experiences with a pathophysiologic mechanism that may cause a poor outcome. A model has been proposed that links preterm labor to a disorder of arousal manifested physiologically as an autonomic hyperreactivity.[25] Future research that relates psychosocial factors to physiologic responses is likely to advance our understanding of stress and adverse outcome.

It is important to note that although life stress is significantly related to outcome, it is not a powerful predictor of complications. Women with high stress levels were 2.3 times more likely to have a complication but nonetheless had a 91% likelihood of a good outcome. Hence, though psychosocial factors are associated with poor outcome, they, like biomedical factors, are not particularly strong predictors.

Nonetheless, these data strongly support a hypothesis that links stressful life events and adverse outcome of pregnancy. Most important, this study showed that serious, clinically significant complications of pregnancy can be related to stressful life changes independent of biomedical risk.

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Commentary

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Since the development of a self-administered instrument to measure stressful life events,[1,2] numerous studies have demonstrated strong associations between psychosocial stress, life change, and illness.[3-9] In early work on these factors and prenatal risk, Nuckolls et al,[10] and later Norbeck and Tilden,[11] incorporated life stress and social support into an interactional model to investigate pregnancy complications. Their findings revealed a higher risk of poor outcomes in women with unfavorable psychosocial assets or emotional disequilibrium, and lent support for the development of a biopsychosocial model for future research. More recently, there has been a recognition of the inadequacy of biomedical risk assessment for the prediction of such events as gestational diabetes and preterm labor, along with a greater appreciation of psychosocial factors in relation to pregnancy complications.[12-16] While the contribution of these factors in explaining the total variance for pregnancy outcome is small, the impact of these studies is reflected in a change in the standard prenatal risk-assessment forms. Newer forms incorporate questions on psychosocial problems, including lack of family support, inadequate resources, and recent loss. (Hollister Maternal/Newborn Record System. Copyright 1986. Hollister Inc, 2000 Hollister Dr, Libertyville, IL 60048; and POPRAS III Prenatal Record. Copyright 1987. American International Perinatal Health Inc, 7960 West Hidden Lakes Dr, Granite Bay, CA 95661.)

While much of the literature has confirmed the negative

impact of psychosocial stress on pregnancy outcome, several studies,[17-20] as noted by Williamson and his colleagues in the preceding paper, have failed to show an effect. In fact, the study by Jones[21] demonstrated a significant association between life change and pregnancy complications that was in the opposite direction from that previously reported, ie, fewer complications among women with greater measured life change. These inconsistencies among prospective studies, particularly for individual psychosocial variables, are likely attributed to problems in conceptualization of the many complexities of stressors and stress moderators, attempts to relate a nonspecific high-risk category to specific outcomes, and the small sample size and varying characteristics of the population under investigation. In addition, a causal assumption between life events and subsequent outcomes may be inaccurate. Gallacher and Gallacher,[24] for example, noted that life events may be as much a consequence of behavior as a determinant.[22] Many paradigms of illness, most from the behavioral literature, focus less on the specific life events encountered than on the individual's ability to adapt or cope with them.[23-27] Magni et al[16] found that pregnancy complications resulted not so much from stress alone as from the interaction of stress with anxiety and coping style. Such concepts have long been accepted within certain fields of medicine, such as microbiology, where illness can be conceptualized as a battle between the virulence of the infectious agent and the host's defenses. It seems logical that accepted constructs of health and illness from both the psychological and the biomedical arena be combined into biopsychosocial models and translated into risk-assessment strategies. A more thorough understanding of the individual's strengths, anxiety, and coping style will clearly be needed, however, before these psychosocial variables, even if adequately measured, can be used for planned interventions.

The above paper by Williamson et al has identified another important problem with current risk-assessment systems: risk is dynamic. Their finding, that women who experienced an increase in their life change score during pregnancy had significantly higher rates of poor outcomes, adds another dimension to the biopsychosocial model. Current risk assessment is too often a process of measurement and categorization into risk groups at one point in time without consideration of changes in that status over time or in response to appropriate intervention. For example, a woman's risk of preterm labor assessed in early pregnancy is no longer relevent when she reaches term. Change variables may prove to be more relevant to certain women, such as those in whom adaptation skills are less developed. This concept of vulnerability in addition to the changing perception of both stress and social support may well take us to the next step in understanding the complex process resulting in health in some and illness in others.

The challenge to future research lies in two major areas. First, an understanding of the mechanisms through which stress operates will increase the ability to predict clusters of outcomes more likely to be associated with specific risks. Pregnancy models under exploration include studies on catecholamines,[28-30] cortisol,[31] and immune function.[32] In hypothesizing linkages to outcomes, chronic or acute elevations of such hormones in response to stress may have detrimental effects on uteroplacental perfusion (resulting in intrauterine growth retardation), glucose tolerance (resulting in macrosomia and/or gestational diabetes), and susceptibility to infection (resulting in chorioamnionitis or the high incidence of pyelonephritis in pregnancy with subsequent preterm labor). While these avenues of investigation may provide us with no more than biochemical markers of underlying disease processes, their usefulness in following interventions could be invaluable.

Second, as the development and refinement of biopsychosocial models in relation to pregnancy outcome may clarify the susceptibility of certain populations of women, better identification of risk for specific outcomes that can be altered by prenatal care and management may result. While intervention trials designed to lower the risk of poor outcomes, such as the use of supportive companions in labor[33] or frequent rest periods for working women to prevent preterm birth,[34] should not be discouraged, better identification of specific subpopulations of unsupported or working women who are truly at risk will provide for more appropriate and cost-effective care. In addition, as it is likely that specific stressful events require particular coping strategies, a better match between coping requirements and the available support will more likely result in better outcomes.[35]

The challenge to medicine and behavioral science is to combine efforts to develop a better understanding of the myriad of factors underlying health and illness. To do so will undoubtedly require a consideration not only of the biological risk factors and the broad areas of life change, anxiety, and social support as dynamic moderators and intensifiers of stress, but also of the socioeconomic and environmental issues that leave certain populations of women at a reproductive disadvantage. Through such efforts, biopsychosocial models can be translated into more predictive risk-assessment instruments. Such instruments will greatly enhance our ability to evaluate specific management strategies that may improve pregnancy outcome.

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