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An Examination of Explanation of Adverse Birth Outcomes

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This article is a reprint of a report which appeared first in the *Nebraska Health Information Project: 1995 Databook*. Dr. Strickland is an epidemiologist at the University of Nebraska Medical Center. Ms. Dietrich is the Prenatal Surveillance System Director at the Nebraska Department of Health and Human Services.

Data archived in the **Nebraska Cancer Registry** are reported in this Brief. These data have been made available to the *Nebraska Health Information Project* by the *Nebraska Health and Human Services System*. More about the Nebraska Health Information Project and about other project reports can be found on page 7 of this document.

Introduction

What can be done to lower the incidence of low birth weight babies? The answer to that question depends on how well we are able to isolate causes of low birth weight, using appropriate research methods. This paper focuses on this issue. Data from the Special Supplemental Program for Women, Infants and Children (WIC) nutritional program are used to improve our ability to measure variables of interest during pregnancies, and to compare results among a population with many similar demographic characteristics.

Data from this study show that young mothers who smoke and gain little weight during pregnancy are much more likely to deliver preterm, low-birth weight babies.

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Introduction

Even though Nebraska's rate of infant mortality returned to its recent level in 1991, falling from 9.1 deaths per 1,000 live births to 7.1 infant deaths per 1,000 live births between 1993 and 1994, infant mortality continues to be a public health concern. Infants born at very low weight (less than 5 pounds), are at greater risk for dying during the first year of life, and those that live may experience a disproportionate amount of adverse health during developmental years. Thus, an important policy question remains: What can be done to lower the incidence of low birth weight babies? The answer to that question depends on how well we are able to isolate causes of low birth weight, using appropriate research methods.

This paper focuses on this issue. Data from the *Special Supplemental Program for Women, Infants and Children (WIC)* nutritional program are used to improve our ability to measure variables of interest during pregnancies, and to compare results among a population with many similar demographic characteristics. The analysis requires isolating the effects of variables found by various investigators to affect low birth weight; the variables include:

- age of the mother
- onset of first prenatal visit during pregnancy
- number of prenatal visits during pregnancy
- nutritional intake during pregnancy
- income of the mother
- race of the mother
- smoking during pregnancy
- education of the mother

Previous studies have shown each of these variables to be related to birth outcomes.

A primary problem is the interdependence of many of these factors. Young maternal age is associated with low education, low income, smoking, poor access to care, and so forth. A comparison of women with low birth weight babies with women with normal babies turns up differences on all these variables and more, and the high intercorrelations make it difficult to determine whether any one factor is more important. If the principal risk factor is a result of a causal pathway, then analysis, particularly of vitals data, becomes very problematic. A recent article covered 20 years of births looking at the association of age and poor outcomes, and restricted to whites in Utah[1]. They found age indeed to be a risk factor, and argued that in Utah there is a lower rate of smoking, alcohol use, and poverty to confound the results. In their discussion, however, they bring up the hypothesis that small maternal stature is the principal risk factor for small infant size, supporting that from the literature.

Small maternal stature may result from both youth and smoking. If those two occur in combination, there could be an interaction, with considerably increased risk of low birth weight. Hediger and colleagues[2] used a knee height measuring device to assess growth in pregnant adolescents compared with older non-growing gravidas. They found that still-growing mothers gained more body mass, but were at higher risk of fetal growth retardation as measured by both birth weight and fetal-placental vascular resistance despite the greater weight gain. They suggest that maternal growth during pregnancy disrupts flow of nutrients to the fetus through increased placental vascular resistance.

High Risk Populations

In situations where multiple factors confound findings, one useful technique is to restrict the sample to the high risk population. This was applied usefully in the first studies of human papilloma virus (HPV) and cervical carcinoma (Koutsky et al.).

Previously, women with cervical carcinoma were compared to control women drawn from the community, in the classic case-control design. Since there are a number of other factors associated with the risk of exposure to HPV, these all differed between cases and controls. Some of these were sexual behavior factors such as age at first intercourse and number of sexual partners, smoking, alcohol consumption, other sexually transmitted diseases (STDs) such as chlamydia and herpes, and so forth. This resulted in many false trails being followed.

The definitive study looked at women in a high risk setting: the STD clinic in a large urban medical center (Harborview Hospital in Seattle), and compared all the infectious agents in women with cervical carcinoma or carcinoma in situ to women matched for age in that same clinic who did not have cervical carcinoma. The results showed no association for the previously seen co-factors, but women with cervical carcinoma were 100 times more likely than those without to show presence of HPV.

In like fashion, we propose investigating low birth weight in a group that is at high risk: the WIC clinic population. These women are enrolled on the basis of low income, and are followed through their pregnancy (from whatever point they enroll) until some time after the infant's birth. Maternal characteristics and habits are recorded at each visit, including smoking habits. Furthermore, through the Pregnancy Nutrition Surveillance System, the WIC records are linked with birth certificates, fetal death certificates, and death certificates, so that information from several sources and on a variety of indicators is available. This presents a very powerful group for examination of risk of low birthweight, and allows examination of behavioral factors such as age and smoking in a group where access to care, income, and education is more uniform, hence minimizing confounding from extraneous variables. We intend to examine the degree of independence of smoking and the strength of smoking as a risk factor for low birth weight, prematurity, and low weight for gestational age within this population. We intend to adjust for, and assess as well, the other variables of interest, in particular young maternal age and small maternal body stature. We hope to be able to assess the degree of independence of these risk factors in a restricted population, and to investigate the possibility of greater-than-additive interaction (i.e. synergy) as well between these factors.

Subjects

The Nebraska Department of Health (NDOH) through its Pregnancy Nutrition Surveillance System (PNSS) collects and analyzes aggregate sociodemographic variables, reproductive risk factors, alcohol and smoking habits, infant feeding practices, and birth outcome information. The information comes from local WIC clinics and is linked at NDOH with the infant's birth certificate. The PNSS program is funded by the Centers for Disease Control and Prevention (CDC), and all data are submitted to them. The CDC funds PNSS programs in 34 states, each designed to collect a standardized set of information from WIC programs.

WIC is a program intended to give nutritional support both during and after pregnancy to women and infants who are at risk of poor nutrition because of poverty. There is a means test for entry to the program, with a top cutoff of 180 percent of the Federal Poverty Line. Therefore, the population is not representative of the general population of women in their reproductive years, but is more narrowly selected in income levels, and in education and access to health care as well. This is an advantage for researching this topic, since possible confounding resulting from large differentials in access to services is reduced.

The current research uses information collected in 1992 and 1993, and includes considerably more detailed information than is available on birth certificates. Specifically, height and weight of the mother are measured, and smoking information including amount is asked for three points in time - three months before pregnancy, during, and three months after delivery. There were 5,805 women in this sample.

Individual data are collected in the course of patient interview at the WIC clinics across the state by dietitians and nurses staffing the clinics. While data collection forms are standard, these are clinics rather than survey centers, and hence standard interview protocol such as would be expected in an epidemiologic study is not followed. This means there may be interviewer biases in how much information is obtained. While we would hope these biases would be random and unrelated to the hypotheses of interest, there is no way to ascertain that in the absence of quality control protocols.

Results

Mean age of the mothers was 24 (standard deviation (SD) 5.3, range 13 to 46), mean monthly household income was $913 (SD $555.30, range $0 to $4,350), and mean grades of school completed was 11.9 (SD 2.0, range 1 to 21). Various racial and ethnic groups were represented in the sample, as shown in **Table 1** below.

TABLE 1
Racial and Ethnic Characteristics of the Mothers

Group	Number	Percent
White	4,414	76.0%
Black	691	11.9%
Hispanic	513	8.8%
Native American	94	1.6%
Asian	86	1.5%
Other	7	0.1%
	5,805	**99.9%**

On the whole, this was a group of healthy mothers and infants, but there were some premature and low birth weight infants. Gestational age was estimated from date of last menstrual period.

Table 2 outlines mean birth weight by categories of gestational age, followed by mean gestational age by categories of birth weight in **Table 3**.

TABLE 2
Mean Birth Weight by Gestational Age

Weeks of Gestation	Mean Birth Weight in Grams	Number of Births
Less than 32	1,797.7	34
32-34	2,350.3	75
35-37	2,734.7	328
38-42	3,411.2	3,849
Greater than 42	3,356.0	1,486
Total	**3,335.2**	**5,772**

TABLE 3
Mean Gestational Age of Infants by Birth Weight

Birth Weight in Grams	Mean Gestation (Days)	Number Of Births
Less than 500	282.0	1
500 -15	217.0	31
1500 - 250	255.0	277
2500 - 400	278.0	3,767
Greater than 4000	283.0	520
Total	**276.6**	**4,596**

TABLE 5
Infant's Birthweight in Grams

Mother's Weight Gain	Mean Birth Weight, Grams	Number of Births
Below ideal gain	3,140	1,473
Ideal gain	3,374	2,347
Above ideal gain	3,468	1,555
Unknown	3,300	397
Total	**3,335**	**5,772**

Age, income, education, and smoking were highly predictive of a calculated variable, gravidity minus parity, a proxy for miscarriages and abortions. Predictive of smoking were education and income (both negatively), as well as mother's age (positively). When only smokers were analyzed, age and education were the sole significant predictors of weight gain. Greater maternal age was associated with income, education, and with being married. An important covariate was found to be the mother's weight gain during pregnancy, split into categories of less than ideal, ideal, above ideal, and unknown. See **Tables 4 and 5.**

TABLE 4
Infant's Gestational Age, in Days

Mother's Weight Gain	Mean Gestation	Number of Births
Below ideal gain	274.5	1,256
Ideal gain	277.0	1,966
Above ideal gain	278.1	1,277
Unknown	274.2	97
Total	**276.6**	**4,596**

Models were tested examining the association of mother's age with birth weight, and it was found that the effect of age was largely explained by income. However, the effect of smoking remained strong. One would expect an association between birth weight and gestational age and that indeed was the case in these data.

However, rather than assuming a linear relationship between gestation and birthweight, and entering gestation as a simple linear term, we posit that pre-term babies are a different group than full-term, and that while their low birth weight may be due almost entirely to their prematurity, the birth weight of term babies is related to different factors altogether. Therefore, the sample was divided at gestational age 273 days, the 33rd percentile for this sample.

Further modeling was done separately on each gestational age stratum. For the pre-term babies, low birth weight was explained by smoking, lower body mass index before pregnancy, and a three-way interaction among smoking, weight gain during pregnancy, and mother's age. The results of this model indi-

cate that younger mothers who smoke and who gain less than ideal during pregnancy are at much higher risk of low birth weight babies among those who deliver before day 273.

For the term babies, the important predictors of low birth weight were whether the mother smoked (not how much), her body mass index before pregnancy (positively), and her income (negatively). Her age and her weight gain during pregnancy did not play a role.

Finally, we examined the interaction of mother's age, smoking, and body mass index, as suggested by Fraser et al., and found that interaction did not have a significant effect on birth weight, either overall or when analyzed on the two strata of gestational age.

One weakness of data of this type is uncertainty of gestational age, which is calculated from the mother's recall of the date of her last menstrual period (LMP). Intuitively, one would expect ability to recall LMP to be randomly distributed and not to affect results.

However, Klebanoff et. al.,[3] found in a sample of Danish women that uncertainty in LMP was associated with being employed, low SES, second or later births, and smoking more than 20 cigarettes daily. This bias could enter into our results, especially in the pre-term babies, where age and smoking were important. Klebanoff points out that uncertainty was more common when the birth was 'nominally pre-term,' a good description of our cutoff point for pre-term.

Therefore, the risk factors seen in the pre-term babies for low birth weight could easily be risk factors for uncertain LMP, since that group likely has a larger proportion of such uncertainty. Those associations therefore should be interpreted cautiously.

References

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