Secular Trends in the Rates of Preeclampsia, Eclampsia, and Gestational Hypertension, United States, 1987–2004

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BACKGROUND
Few studies have reported on population-level incidence of or trends in the hypertensive disorders of pregnancy, and none report on data through 2004. We describe population trends in the incidence rates of preeclampsia, eclampsia, and gestational hypertension in the United States for 1987–2004.

METHODS
We analyzed public-use data from the National Hospital Discharge Survey (NHDS), which has been conducted by the Centers for Disease Control and Prevention, National Center for Health Statistics since 1965. We calculated crude and age-adjusted incidence rates and estimated the risk associated with available demographic variables using Cox regression modeling.

RESULTS
Rates of preeclampsia and gestational hypertension increased significantly (by 25 and 184%, respectively) over the study period; in contrast, the rate of eclampsia decreased by 22% (nonsignificant). Women under the age of 20 were at significantly greater risk for all three outcomes. Women in the south of the country were at significantly greater risk for preeclampsia and gestational hypertension when compared to those in the Northeast.

CONCLUSIONS
The increase in gestational hypertension may be exaggerated because of the revised clinical guidelines published in the 1990s; these same revisions would likely have reduced diagnoses of preeclampsia. Therefore, our observation of a small but consistent increase in preeclampsia is a conservative indication of a true population-level change.


Preeclampsia is a dangerous, multisystem complication of human pregnancy and a leading cause of fetal and maternal morbidity and mortality worldwide. This hypertensive disorder of pregnancy is characterized by sustained de novo hypertension and proteinuria after 20 weeks of gestation. The maternal syndrome is associated with pitting edema, particularly of the hands, face, and feet, abnormal clotting, and endothelial abnormalities, as well as liver and renal dysfunction. With progression of preeclampsia to eclampsia or occurrence of HELLP (Hemolysis, Elevated Liver enzymes, Low Platelets) syndrome, the risk of maternal death increases. The fetal syndrome can be manifested as preterm delivery, growth restriction, placental abruption, fetal distress, and in some cases, death, especially with onset of preeclampsia before 34 weeks of gestation. It is important to note that preeclampsia is the underlying cause of about one-quarter of all medically indicated preterm deliveries in the United States.1 Because preeclampsia is a multisystem disorder that can progress rapidly, it requires prompt intervention that may include observation in a tertiary care setting and induction of delivery, which is the only known cure for this condition.2–4

Epidemiologic research suggests that preeclampsia has a multifactorial etiology that includes an immunogenetic component.5 Established risk factors include nulliparity, family history of preeclampsia–eclampsia, preeclampsia in a previous pregnancy, obesity, increased insulin resistance, hyperlipidemia, increased trophoblastic mass (i.e., multiple gestation, molar pregnancy), and change of sexual partner between pregnancies.5 Protective factors include a prior completed pregnancy and a terminated pregnancy for women conceiving again with the same partner.6

In a previous publication, our group summarized nationally representative data on the incidence of preeclampsia and eclampsia from 1979 through 1986.7 A subsequent publication by Zhang et al. provided an update from the years 1988 through 1997.8 There is now a pressing need to update these
reports so as to track changing rates and observe trends that may be related to population-level increases in pre-pregnancy obesity,10 diabetes,11 maternal age,12 and multiple births12 or changing social and economic conditions that may affect access to health care.

In this article, we present trends in incidence rates and selected demographic risk factors during 1987–2004 so as to provide continuity with our earlier publication and enable observation of long-term trends. Knowledge of these trends at the population level should improve understanding of maternal risk, encourage preconception and interconception counseling, and increase appropriate monitoring and treatment, particularly for high-risk women.

**METHODS**

**Definitions.** Gestational hypertension is defined as sustained high blood pressures of 140 mm Hg systolic or 90 mm Hg diastolic with onset after the 20th week of gestation in women with no history of chronic hypertension and where evidence of proteinuria is absent. Chronic hypertension is diagnosed if hypertension is present before the 20th week of gestation or when blood pressure does not return to normal by 12 weeks postpartum.12,13

Current criteria for a diagnosis of preeclampsia require the presence of de novo hypertension and proteinuria with onset after the 20th week of gestation.2,13 Eclampsia is the presence of seizures in a woman with preeclampsia when the seizures cannot be attributed to other causes.2,13

**Data source.** We obtained data for this study from the National Hospital Discharge Survey (NHDS) public-use data set. This annual survey, which has been conducted by the National Center for Health Statistics since 1965, uses a nationally representative sample of discharge records drawn from a probability sample of ~400 non-Federal, short-stay hospitals in all 50 states and the District of Columbia (military, veteran, and institutional hospitals are excluded). The NHDS was redesigned in 1988 to provide geographic sampling comparable to other National Center for Health Statistics surveys.14 The redesign ensured inclusion of all hospitals with at least 1,000 beds and 40,000 or more discharges annually. The sampled discharge records are weighted to represent the total number of discharges from non-Federal short-stay hospitals in the United States. Estimates based on fewer than 30 records are considered to be statistically unreliable.14

Discharge diagnoses from the NHDS are coded according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). Up to seven discharge diagnoses and four operative procedures are abstracted from the face sheet of each hospital record sampled. Additional data items collected include the patient’s date of birth, sex, race, marital status, expected source of payment for hospitalization, and geographic region of residence. It should be noted that the ICD-9-CM codes are assigned by the individual sampled hospitals according to their own procedures. NHDS data are subject to computerized edits and manual review, including validity and range checks for non-medical variables and consistency checks for dates and ICD-9-CM codes. The National Center for Health Statistics reports high accuracy of discharge diagnostic categories in comparison with hospital census reports.14

**Study population.** The study population included all NHDS-sampled discharges for delivery admissions among women who delivered one or more live or stillborn infants between 1987 and 2004. Hospital admissions for which a delivery occurred were identified by the ICD-9-CM code V27. In 2004, the NHDS represented ~4.1 million hospitalizations for delivery with an average length of stay of 2.6 days.15

**Analytical methods.** Crude and age-adjusted incidence rates were calculated as cases per 1,000 deliveries for gestational hypertension (ICD-9-CM 642.3), mild or unspecified preeclampsia (ICD-9-CM 642.4), severe preeclampsia (ICD-9-CM 642.5), and eclampsia (ICD-9-CM 642.6). For the analysis, mild or unspecified preeclampsia and severe preeclampsia were combined into a single variable (preeclampsia). Direct standardization was conducted to adjust incidence rates for the effects of maternal age using the 1995 US natality population, which represents the mid-point of the 18-year study period. Weighted linear regression was used to test for linear trend in the crude and age-adjusted rates of all preeclampsia (ICD-9-CM 642.4 and 642.5) and gestational hypertension (ICD-9-CM 642.3) over the period, 1987–2004. Because eclampsia is a relatively rare complication of pregnancy, we calculated average annual age-adjusted rates for two 9-year time periods so as to ensure statistical stability of these estimates.

In addition to diagnoses and operative procedures, the NHDS public-use data set includes patient’s date of birth, sex, marital status, expected source of payment, and geographic region of residence. Although race and marital status are of great interest, we were not able to use them in our analysis because of the large proportion (>50%) of “unknown” and “other” responses in the NHDS data set. Rate ratios were calculated to estimate the risk of all gestational hypertension, preeclampsia, and eclampsia associated with maternal age and geographic region of the sampled hospitals. Rate ratios for preeclampsia and gestational hypertension were calculated on the basis of five age categories (i.e., <20, 20–24, 25–29, 30–34, 35+); for eclampsia, sample size limitations restricted the analysis to just two age categories (i.e., <20, ≥20). In calculating rates, we used Cox regression modeling to simultaneously adjust for maternal age and geographic region.16 Because of concerns about confidentiality, the NHDS public-use data set does not include the sampling stage variables. Therefore, in order to take into account the complex sampling design of the NHDS, we assumed, on the basis of previous empirical results, that the estimated variance under NHDS is twice as large as that under simple random sampling.17

**Protection of human subjects.** This study used de-identified public-use data that did not involve human subjects; therefore, institutional review board approval was not required.
RESULTS

The crude average annual incidence rates (cases per 1,000 deliveries) of preeclampsia and gestational hypertension over the 18-year study period were 27.4 and 21.3, respectively (data for individual years are shown in Table 1); for eclampsia, the rate was 0.92.

The rate of preeclampsia and gestational hypertension increased significantly over the 18-year study period (Figure 1). The age-adjusted rate (per 1,000 deliveries) of preeclampsia rose by 24.6% from 23.6 in 1987–1988 to 29.4 in 2003–2004. Over the same time period, the rate of gestational hypertension nearly tripled from 10.7 to 30.6. In contrast, the age-adjusted rate of eclampsia decreased by 22.0% from an average annual rate of 1.04 during 1987–1995, to 0.82 during 1996–2004. These two rates did not differ statistically, but the NHDS is not powered to detect modest changes in the occurrence of rare conditions.

Shown in Table 2 are the number of weighted cases, crude incidence rates, and relative risk estimates of preeclampsia, gestational hypertension, and eclampsia associated with maternal age and geographic region, each adjusted for the effects of the other variable. When compared to women ages 30–34, the risk of preeclampsia is consistently and significantly higher among women <25 years of age and highest among women <20 years of age; the risk among women of ages ≥35 is slightly higher and comparable to that of women in the 20–24-year age group. Regional analyses show that the risk of preeclampsia is significantly higher for women delivering in the south of the country, while women delivering in the west are at the lowest risk. During the second 9-year time period of the study, the risk of preeclampsia is lower in each of the geographic areas relative to the northeast.

Women <20 years of age are at significantly increased risk of gestational hypertension. Women ≥35 years of age were also at increased risk, although this rate ratio was not statistically significant. In all sub-categories of maternal age and geographic area, the rates of gestational hypertension increased uniformly over time (Table 2).

![Figure 1: Age-adjusted incidence per 1,000 deliveries for women with gestational hypertension ($b = 0.0024; P < 0.0001$) or preeclampsia ($b = 0.0009; P = 0.009$) for 2-year periods, 1987–2004.](image-url)
Women <20 years of age had a 2.6-fold higher risk of eclampsia than older women during the first time period of the study, and a slightly lower risk during the second time period. In our regional analysis, the risk of eclampsia was higher in the south than in the northeast (reference) during the first time period. The risk for women whose deliveries took place in the midwest was comparable to the risk for women in the northeast, whereas the risk was lowest for those in the west. During the second time period, the risk in all three regions had decreased to levels more comparable to or lower than those observed in the northeast (Table 2).

**DISCUSSION**

Our analysis indicates that important population-level changes in the rates of preeclampsia, eclampsia, and gestational hypertension occurred during the 18-year period ending in 2004. The rates of both preeclampsia and gestational hypertension increased significantly. In contrast, the eclampsia rate showed a nonsignificant decrease of 22% over the same time period.

This study is important because few others have reported incidence rates based on population-level data, and none reflect the results of analysis carried out through 2004, the latest year for which NHDS data are available. The NHDS data...
set is remarkable for its depth in terms of national representation of US short-stay hospitals and its breadth in providing annual data on hospital discharges since 1965. The incidence rates we report for preeclampsia are similar to those reported from other population-based studies in the United States, Canada, and western Europe, range from 2 to 5%.

Rates as low as 1.1% and as high as 7.5% have been reported from regional, clinical, and multicenter trials; however, the generalizability of these data is limited by the selective representation of hospitals and study populations.

It is interesting to note that our data indicate higher rates of eclampsia than those reported from population-based studies in Canada, the United Kingdom, and western Europe, with lowest rates (per 1,000 deliveries) ranging from 0.24 in Finland and 0.27 in Nova Scotia to 0.44 in Sweden, and 0.66 in Scotland. Any possible explanations for these differences in international data are speculative because of the very low incidence of this condition, but may include: international and temporal variation in definitions and classification of hypertensive disorders of pregnancy; the possibility of greater misclassification of preeclampsia as eclampsia in the sampled US hospitals; racial and ethnic differences among the populations; and the presence of universal health care outside the United States, which may provide greater opportunity for earlier detection and treatment of preeclampsia.

Despite the acknowledged strengths of the NHDS sample and our analytical methods, our conclusions may be constrained by certain limitations of the data set. Recent validation studies of hospital discharge diagnoses of obstetrical health conditions conducted in the United States and Europe indicate moderate to high validity for all diagnoses of preeclampsia and gestational hypertension. A recent study of the Danish registry data reviewed the hospital charts of 3,039 deliveries and reported a positive predictive value of 74.4% for all preeclampsia diagnoses. Another recent study reported the potential for under-representing of deliveries with severe complications if estimates are identified only by the maternal delivery code (V27); the authors recommend an enhanced algorithm for improving estimates. Because NHDS is based on discharges (not individuals), we were restricted to using only the V27 code to identify cases, in order to minimize the probability of counting a single mother more than once.

A limitation of the NHDS data that is particularly relevant to reproductive health research is the high proportion of missing information on the variables “maternal race” and “marital status”, making them insufficient for valid analysis. In addition, the NHDS does not collect data on parity, reproductive history, and other established risk factors for preeclampsia, including pre-pregnancy body mass index, family history of preeclampsia, and health behaviors such as smoking. The NHDS is also limited by its sample size, which may not permit detection of modest and yet important changes in the occurrence of rarer outcomes, such as eclampsia.

We should also note that in 1996, and again in 2002, the American College of Obstetricians and Gynecologists adopted new clinical guidelines and terminology, respectively, for classifying the hypertensive disorders of pregnancy. The American College of Obstetricians and Gynecologists’ 1996 Technical Bulletin provided stricter and more specific definitions of preeclampsia than those previously recommended, requiring that cases meet criteria for hypertension in the presence of proteinuria after the 20th week of gestation. In 2002, the American College of Obstetricians and Gynecologists adopted the recommendations of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy to use the term “gestational hypertension” rather than “transient hypertension of pregnancy” for a patient with hypertension with no evidence of proteinuria; the latter term is now reserved for patients in whom a definitive diagnosis is made by 12 weeks postpartum. A logical consequence of the stricter 1996 criteria for a diagnosis of preeclampsia would be a proportional increase in diagnoses of gestational hypertension, some of which would have previously met American College of Obstetricians and Gynecologists criteria for preeclampsia, as observed in our study. This change in diagnostic guidelines may also have resulted in a decrease in diagnoses of preeclampsia; therefore, the increase we report in preeclampsia is likely to represent a true increase in the incidence of this condition.

What are the possible causes of the substantial increases we found in rates of preeclampsia and gestational hypertension? There are several plausible contributors, among them, population-level increases in known risk factors for preeclampsia such as pre-pregnancy overweight and obesity, diabetes, multiple births, and maternal age. Our analysis of the risk of preeclampsia by geographic region suggests that risk is highest among women residing in the south, possibly because of the higher prevalence of obesity and the higher proportion of women of black race in that region, neither of which could be assessed because of limitations in the data set. An alternative explanation may be related to climatic differences across US regions. Some studies have reported a higher incidence of preeclampsia associated with conception during the spring and summer months. Potential mechanisms include seasonal variation in exposure to infections, dietary changes, and alteration in vitamin D regulation and calcium metabolism as a consequence of exposure to sunlight, which are, in turn, associated with blood pressure levels. Year-round temperatures and sunlight exposures in the southern latitudes are higher when compared to temperate regions; the possibility exists that these climatic characteristics are related to the observed higher incidence of preeclampsia in the south. Though not statistically significant, the decreased rate of eclampsia reported in this study is encouraging. This finding may reflect better and earlier diagnosis of preeclampsia, resulting in prompter treatment and prevention of eclampsia. The reduction in risk for women under 20 may similarly reflect increased clinical awareness of young maternal age as a risk factor, and the decrease in teen birth rate that occurred over the 18-year study period. Analysis of eclampsia risk by geographic region indicates that regional differences that
were present in the first nine-year time period had diminished, thereby suggesting that prevention efforts have become increasingly successful across the country. The reduction of risk in the south is most notable.

The observed increases in the incidence of preeclampsia and gestational hypertension represent important changes in the burden of maternal morbidity at the population level, raising both clinical and public health concerns. These study findings should serve as an important call for clinicians to heighten their awareness of the increased population-level risk for hypertensive disease originating in pregnancy. An increase in the risk for conditions as potentially dangerous as preeclampsia and eclampsia underlines the importance of regular reproductive health care during the preconception, antenatal, and interconception periods. Continued epidemiological research should focus on uncovering preventable causes of preeclampsia, while public health practice and policy must promote improved access to health care prior to conception as well as during gestation and between pregnancies, and reduction of social and behavioral risk factors, including overweight and obesity.

Disclosure: The authors declared no conflict of interest.