DESCRIPTIVE AND CLINICAL EPIDEMIOLOGY OF PREECLAMPSIA AND ECLAMPSIA IN FLORIDA

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Objective: To calculate preeclampsia/eclampsia rates for Florida and identify risk factors for prolonged length of stay (PLOS) among women hospitalized throughout Florida for preeclampsia/eclampsia and discharged in 2001.

Design: Analyses were performed using a statewide hospital discharge dataset from Florida. Hospital discharge rates per Florida female population and risk per 100 deliveries were calculated for women hospitalized for preeclampsia. Binomial regression was used to calculate relative risks (RR) of PLOS among 5495 women. Generalized estimating equations were used to account for nesting by facility.

Results: Non-Whites had higher preeclampsia discharge rates per 10,000 population than Whites in every age group. The overall risk of preeclampsia was 3.9 per 100 deliveries, with the highest risks in the youngest and oldest age groups. The strongest risk factor for PLOS was having a diagnosis of preeclampsia/eclampsia superimposed on pre-existing hypertension. These patients had 2.64 times the risk of PLOS than patients who had mild or unspecified preeclampsia (*P* value $<.0001$.) Diabetics were also at a higher risk of PLOS (adjusted RR=1.26, *P*=.003). Women who were admitted from the emergency department were 26% less likely than women admitted from other sources to have PLOS (adjusted RR=.74, *P*=.01). For every 10-year increase in maternal age, there was a 23% increase in the risk of PLOS (adjusted RR=1.23, $P<.0001$).

Conclusions: Advancing maternal age, Black race, diabetes, severe preeclampsia, and preeclampsia (or eclampsia) superimposed on existing hypertension increased the risk of PLOS, while being admitted from the emergency department was associated with a decreased risk of PLOS. (*Ethn Dis*. 2007;17:736–741)

Key Words: Preeclampsia, Length of Stay, African Americans

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INTRODUCTION

Preeclampsia is a disorder unique to pregnancy and characterized by several factors including hypertension and proteinuria.[1] It is a major contributor to a poor pregnancy outcome.[2] Women with preeclampsia are at risk for several adverse conditions including convulsions, abruptio placentae, disseminated intravascular coagulation, and cerebral hemorrhage.[3] Preeclampsia is also a risk factor for neonatal death and conditions such as severe growth retardation, hypoxemia, and premature birth.[3] Risk factors for hypertensive disorders of pregnancy include Black race,[4] obesity, and extremely young or advanced maternal age.[3]

Large regional databases may assist investigators in elucidating geographical trends in preeclampsia incidence and ascertaining correlates of outcomes among women hospitalized for this condition. The goals of this study were to calculate age- and race-group specific preeclampsia hospital discharge rates for Florida, calculate age- and race-group specific preeclampsia rates per 100 deliveries, and identify predictors of a prolonged length of stay (PLOS) using a statewide hospital discharge database. These types of datasets allow investigators to conduct rapid, population-based analyses. A PubMed search did not reveal any similar studies that had been conducted using Florida inpatient data.

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MATERIALS AND METHODS

Source Population

Retrospective analyses were performed using a hospital discharge dataset that was obtained from the Florida Agency for Health Care Administration (Tallahassee, Florida). This public-use database includes discharge summaries from all non-federal Florida hospitals except state tuberculosis and state mental health hospitals. After data are entered into this system, they are subjected to formatting and logic checks. The primary hospital submitting patient information must then certify the data are correct and verify the accuracy of a summary report before it is released by the Agency for Health Care Administration.

This dataset contained clinical and demographic information for 2,343,330 patients who were hospitalized for at least one day and discharged in calendar year 2001. The principal diagnosis and up to nine secondary diagnoses were coded using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Up to and including 10 procedures (a principal procedure field plus nine secondary procedures) could have been recorded. Procedures were coded using the ICD-9-CM.

Definition of Preeclampsia and Eclampsia

Records were included in our analysis if the principal diagnosis was preeclampsia or eclampsia. Preeclampsia and eclampsia were defined as ICD-9-CM code 642.40, 642.41, 642.42, 642.43, 642.44, 642.50, 642.51, 642.52, 642.53, 642.54, 642.60, 642.61, 642.62, 642.63, 642.64, 642.70, 642.71, 642.72, 642.73, or 642.74.

Statistical Analysis: Rates

The following age categories were created (in years): 10 to 19, 20 to 29, 30 to 39, 40 to 49, and 50 to 54. Age-group specific hospital discharge rates for Florida residents were calculated by the dividing the appropriate number of cases that were discharged in 2001 by the stratum-specific female Florida population estimate for 2001. Population estimates were available from the Florida Department of Health's website for two races, White and non-White.[5] These estimates did not consider Hispanic ethnicity. We calculated rates for White women (White non-Hispanic and White Hispanic) and for non-White women (Black, Black Hispanic, Asian or Pacific Islander, American Indian/Eskimo/Aleut, and other). A more detailed classification of race and ethnicity was possible during our regression analyses as described below.

A total of 5622 cases were initially identified. A small proportion of the patients (n=60, 1.1%) was not Florida residents or had an unknown county of residence and hence was excluded from the calculations. Two percent of the cases had unknown values for race and therefore had to be deleted. The final sample size was 5453.

Hospital discharge rates summarize the burden of the condition in the population. A peak in the discharge rate in a particular age group may simply reflect a large number of deliveries in that age group rather than an increased risk of preeclampsia. To calculate the risk of preeclampsia, we divided the number of cases of preeclampsia by the number of deliveries in that particular age-race group. Deliveries were enumerated using ICD-9-CM procedure codes. If a patient had any of the following procedure codes in any of her 10 procedure fields she was considered to have delivered a child during that admission: 72, 72.1, 72.21, 72.29, 72.31, 72.39, 72.4, 72.51, 72.52, 72.53, 72.6, 72.71, 72.79, 72.8, 72.9, 72.9, 73.3, 73.59, 74, 74.1, 74.2, 74.4, 74.99.

Statistical Analysis: Regression

A retrospective cohort study was conducted to identify correlates of PLOS. PLOS was defined as a length of stay (recorded in days) that was greater than the 75th percentile in our sample. A length of stay of five days represented the 75th percentile in our study. Dichotomizing length of stay using the 75th percentile has been used in previous clinical epidemiology analyses.[6,7]

Data were analyzed using The SAS System for Windows 9.1 (The SAS Institute, Inc., Cary, North Carolina). We performed binomial regression[8] to determine if the following variables were associated with PLOS: principal discharge diagnosis, age (in years), race/ethnicity, health insurance status, source of admission, and diabetic status. Principal discharge diagnosis was a four-level categorical variable: mild or unspecified preeclampsia (ICD-9-CM code 642.4), preeclampsia or eclampsia superimposed on pre-existing hypertension (ICD-9-CM code 642.7), severe preeclampsia (ICD-9-CM code 642.5), and eclampsia (ICD-9-CM code 642.6). Race/ethnicity was originally an eight-level variable (seven racial ethnic groups plus a category for missing). This variable was converted to a four-level categorical variable: White Hispanic, Black non-Hispanic, other racial/ethnic group, and White non-Hispanic (referent). Due to the small numbers of Asian and Pacific Islanders, Black Hispanics, American Indians/Eskimo/Aleut, and patients of other racial/ethnic groups, these categories were collapsed into a new other group. Our health insurance variable was created using the principal payer variable found in the database. Patients who had commercial health insurance were compared to other patients. Commercial health insurance was defined as commercial insurance including health maintenance organizations and preferred providers organizations. The referent category included several groups including Medicare and Medicaid beneficiaries, Veteran's Affairs, and charity. The "source of admission" variable was originally a nine-level variable (eight sources plus a ninth category for unknown/unavailable source of admission). It was converted to a binary variable: admitted from the emergency department versus other source such as a referral from the patient's personal physician or a hospital transfer. A small number of patients (n=17) who had an unknown source of admission were not included in the regression analyses. Diabetes was defined as the presence of ICD-9-CM code 250.0 to 250.9 (type 1 and 2 diabetes) or ICD-9-CM code 648.8 (gestational diabetes) in any of the secondary discharge diagnosis fields. Seven patients were found to have both an ICD-9-CM code for gestational diabetes and the ICD-9-CM code for either type 1 or type 2 diabetes. These patients were included in the regression analyses, but for descriptive purposes they were treated as diabetic patients of unknown type/category.

Approximately 71% of the women in our study delivered during their hospital stay. Delivering during the current admission was associated with PLOS in a univariate regression model (data not shown), and therefore this variable was not included in our multiple binomial regression model. It was most likely in the causal pathway between two of our predictors, the principal discharge diagnosis and emergency department admission, and the outcome of PLOS. For example, women who are experiencing eclampsia may be more likely to be delivered, which in turn is related to the outcome of PLOS. Adjusting for variables in the causal pathway is avoided in the practice of epidemiology.[9,10]

In the setting of a cohort study, binomial regression yields relative risk estimates while logistic regression would yield incidence odds ratios. Crude and adjusted relative risks (RR) for PLOS were calculated using the GENMOD procedure in SAS.[8] An RR was considered statistically significant if the 95% confidence interval for the population RR excluded the null value of one.

After deleting records with missing values for the any of the independent variables or dependent variable, a total of 5495 records were available for the binomial regression. This portion of the study included a small number of women (n=59) hospitalized in Florida for preeclampsia who were not residents of Florida or whose county of residence was not known.

Patients within a particular facility may have a similar risk of PLOS due to the overlap in providers and treatment philosophy, and therefore the assumption of statistically independent observations was most likely violated. To clarify, each patient in our study was not hospitalized in a different hospital; that is, 5495 women hospitalized in 5495 unique facilities. Instead this population of preeclamptic/eclamptic patients was nested within 127 of Florida's reporting hospitals. Failure to adjust for this correlation may affect point estimates and confidence intervals. We employed generalized estimating equations to account for potential correlations between patients treated at the same hospital.[11] This technique ensures that confidence intervals for RRs are not falsely narrower and that *P* values are not spuriously smaller (closer to zero) when one analyzes clustered data. An exchangeable correlation structure was specified.[12]

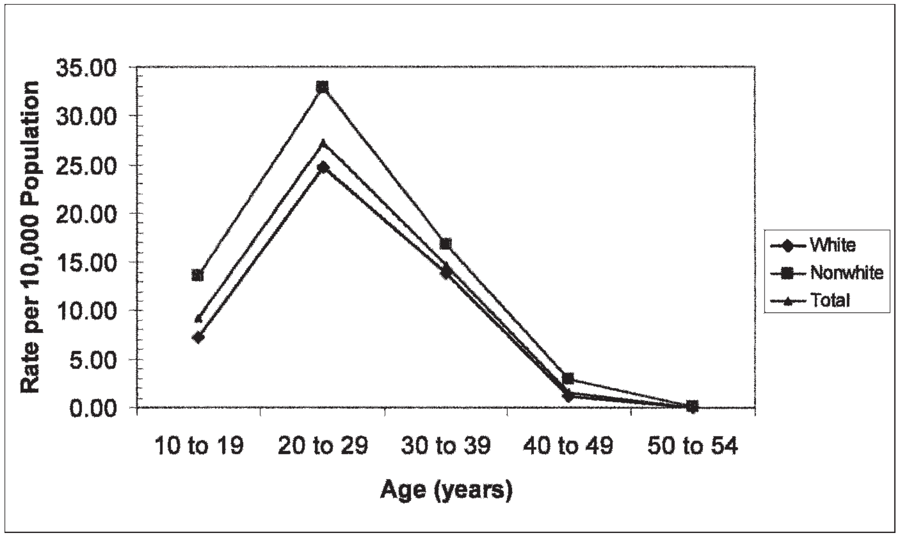

Fig 1. Preeclampsia/eclampsia hospital discharge rates by age and race, Florida, 2001

This study was approved by the institutional review board of the Texas Tech University Health Sciences Center School of Medicine at El Paso, El Paso, Texas.

RESULTS

State discharge rates for preeclampsia/eclampsia are shown in Figure 1. As described above, this portion of the analyses was limited to two racial groups since Florida population estimates were available for only Whites and non-Whites and did not distinguish between those of Hispanic ethnicity and those who were not of Hispanic ethnicity. For both racial groups, the hospital discharge rate peaked in the 20- to 29-year age group. In the 40- to 49-year age-group, the non-White rate was 2.4 times that of the White rate: 2.90 per 10,000 population vs 1.21 per 10,000 population.

Figure 2 displays the risk of receiving a principal discharge diagnosis of preeclampsia or eclampsia by age and race among women hospitalized throughout Florida and discharged in 2001. For each age and race group, the number of cases was divided by the number of deliveries. The overall rate was 3.9% (5453 cases/140,192 deliveries). Mothers in the youngest and oldest age categories were at the highest risk of developing preeclampsia or eclampsia.

The median age of the patients was 26 years (Table 1). White non-Hispanics and Blacks combined made up 77% of the study sample. Approximately 13% of the patients were admitted from the reporting facility's emergency department. Almost 8% of the patients were diabetic, and most were classified as gestational diabetics. The hospital mortality rate was virtually zero.

Crude and adjusted RRs for PLOS are reported in Table 2. In the crude (unadjusted) analysis the strongest risk factor for PLOS was having a diagnosis of preeclampsia/eclampsia superimposed on pre-existing hypertension. These patients had more than three times the risk of PLOS than patients who had mild or unspecified preeclampsia (RR=3.16, *P* value <.0001). This strong association persisted after controlling for several clinical and demographic variables. Diabetics in the crude analysis were 65% more likely than nondiabetics to have

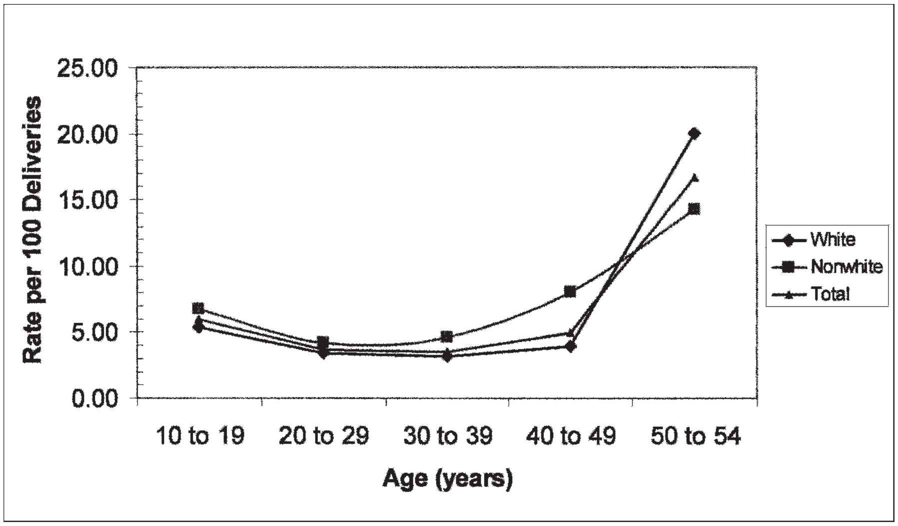

Fig 2. Risk of preeclampsia/eclampsia per 100 deliveries by age and race, Florida, 2001. Overall, there were 3487 cases of preeclampsia/eclampsia among White women and 99,324 deliveries. Among non-Whites, there were 1966 cases and 40,969 deliveries overall

PLOS ($P<.0001$). After adjusting for the remaining variables shown in the table, the association between diabetes and the risk of PLOS was weakened but remained statistically significant. Women who were admitted from the emergency department were 26% less likely than women admitted from other sources to have PLOS (adjusted RR=.74, $P=.01$). The RR for maternal age was attenuated but remained significantly elevated after adjustment: for every 10-year increase in age, the risk of PLOS increased by 23% (adjusted RR=1.23, $P<.0001$).

Table 1. Demographic and clinical characteristics of patients hospitalized for preeclampsia or eclampsia (*n*=5495)

	n **(%) or Median (Range)**
Principal discharge diagnosis	
Eclampsia, *n* (%)	210 (3.8)
Severe preeclampsia, *n* (%)	1697 (30.9)
Preeclampsia or eclampsia superimposed on pre-existing hypertension, *n* (%)	545 (9.9)
Mild or unspecified preeclampsia, *n* (%)	3043 (55.4)
Age in years, median (range)	26 (12–50)
Length of stay in days, median (range)	3 (1–52)
Prolonged length of stay (>5 days), *n* (%)	902 (16.4)
Race/ethnicity	
White Hispanic, *n* (%)	1037 (18.9)
Black non-Hispanic, *n* (%)	1763 (32.1)
White non-Hispanic, *n* (%)	2474 (45.0)
Other racial/ethnic group, *n* (%)	221 (4.0)
Commercial health insurance, *n* (%)	2454 (44.7)
Admitted from emergency department, *n* (%)	730 (13.3)
Diabetic, *n* (%)	429 (7.8)
Type 1 diabetes, *n*	47
Type 2 diabetes, *n*	39
Gestational diabetes, *n*	336
Unclear/unknown diabetic type/category, *n*	7
Died in hospital	1 (0.02)

DISCUSSION

We undertook an examination of the descriptive epidemiology and clinical epidemiology of preeclampsia/eclampsia in Florida. The results of the descriptive portion of our study agree with national data. For example, the incidence of pregnancy-related hypertension in the United States in 2001 was 3.8 per 100 live births.[13] We report a preeclampsia/eclampsia rate of 3.9 per 100 deliveries. Our median length of stay (Table 1) was 3 days and the mean was 4.1 days. According to the 2001 US Nationwide Inpatient Sample, the average length of stay of women treated for hypertension complicating pregnancy was 3.4 days.[14]

The second portion of our investigation was an analytic study. To our knowledge this is the first published epidemiologic study of PLOS among women hospitalized in Florida for preeclampsia. A strength of this analysis is its use of a population-based database that captured discharges from most Florida hospitals in 2001. We found that advancing maternal age, Black race, diabetes, severe preeclampsia, and preeclampsia (or eclampsia) superimposed on existing hypertension increased the risk of PLOS, while the source of admission (admitted from the emergency department compared to other categories) decreased the risk of PLOS (Table 2).

We report a preeclampsia/eclampsia rate of 3.9 per 100 deliveries.

Table 2. Crude and adjusted relative risks for prolonged length of stay from binomial regression models using generalized estimating equations (*n*=5495)

Potential Risk Factor	Crude			Adjusted		
	Relative Risk	95% CI	*P* value	Relative Risk	95% CI	*P* value
Principal discharge diagnosis						
Eclampsia	1.28	.84–1.95	.25	1.42	.93–2.17	.10
Severe preeclampsia	2.59	2.18–3.08	<.0001	2.50	2.10–2.97	<.0001
Preeclampsia or eclampsia superimposed on pre-existing hypertension	3.16	2.33–4.30	<.0001	2.64	1.92–3.63	<.0001
Mild or unspecified preeclampsia	1	Referent	–	1	Referent	–
Age (for every 10-year increase)	1.41	1.29–1.54	<.0001	1.23	1.12–1.35	<.0001
Race/ethnicity						
White Hispanic	.99	.84–1.17	.89	1.07	.90–1.27	.44
Black non-Hispanic	1.23	1.03–1.46	.02	1.20	1.01–1.41	.03
Other race/ethnicity	1.00	.68–1.47	1.00	1.02	.69–1.51	.93
White non-Hispanic	1	Referent	–	1	Referent	–
Commercial health insurance						
Yes	1.21	1.03–1.43	.02	1.06	.90–1.24	.48
No	1	Referent	–	1	Referent	–
Source of admission						
Emergency department	.61	.43–.88	.01	.74	.58–.94	.01
Other source	1	Referent	–	1	Referent	–
Diabetic						
Yes	1.65	1.41–1.94	<.0001	1.26	1.08–1.46	.003
No	1	Referent	–	1	Referent	–

CI= confidence interval.

The protective effect of being admitted from the emergency department merits further discussion. At first glance this result appears counterintuitive. One may expect that patients admitted from the emergency department have severe disease and therefore may have longer stays than other patients; however, this variable may simply be correlated with a rapid delivery secondary to the severity of the condition, which in turn may be correlated with a reduced length of stay. A limited amount of data was available on the timing of procedures, including deliveries, performed during the hospital stay. Up to 10 procedures could be recorded for each patient. Our database only contained information on the number of days that had elapsed between admission and the performance of the principal procedure. If the delivery was coded in the second or higher procedure fields, then we did not know when during the hospital stay the delivery occurred. Ninety-one percent of the deliveries were coded in the principal procedure field. Restricting our sample to women who delivered during their hospital stay and had their delivery coded in the first of their 10 procedure fields, that is, the principal procedure field, we did not find a significant difference in the time to delivery: patients admitted from the emergency department delivered on average one day and six hours after admission, while patients admitted from other sources delivered on average 1 day and 12 hours after admission (P value $>.05$ for both crude and adjusted results). Furthermore, after stratifying the overall dataset by delivery status, we found that among patients who delivered during their hospital stay (n=3883), being admitted from the emergency department was still associated with a reduced risk of PLOS (adjusted RR=.74, P=.04). Among the smaller group of patients who did not deliver during their hospital stay (n=1612), we found no association between the source of admission and the outcome of PLOS (adjusted RR=1.08, P=.78). Both of these RRs were adjusted for the remaining variables shown in Table 2.

We detected a 20% excess risk of PLOS in Blacks even after adjusting for five factors including age, the presence of diabetes, and health insurance status. This racial difference may indicate increased disease severity among Blacks or the presence of residual confounding. Tanaka et al recently reviewed 10 years' worth of New York hospital discharge data.[3] They extracted data on pregnant women whose records included an ICD-9-CM code for a delivery. Tanaka et al found that the prevalence of diabetes was higher among Blacks compared to Whites and that the rate of preeclampsia per 100 hospitalizations with delivery was higher among Blacks than Whites.[3] The racial disparity in PLOS that we report would be best evaluated using a prospective study design. This would allow one to control for additional variables that were not found in our database such as socioeconomic status/income, detailed prenatal care data, and body mass index.

A limitation of this database is the lack of detailed information on parity. Another limitation of the database is that it relies on the providers' assessments and diagnoses of preeclampsia. Although in most cases, the diagnosis of this condition is clear, there are rare instances where even expert providers disagree on whether the patient has preeclampsia or other hypertensive disorders affecting pregnancy such as essential hypertension. Finally, the statewide database lacked a unique patient identifier. Access to a unique patient identification number would have allowed us to determine if there were multiple admissions for any particular patient and then account for these repeated measurements using a random effects parameter or generalized estimating equations. We were, however, able to account for any clustering by hospital. To clarify, women with mild preeclampsia may be discharged and readmitted in a few weeks. It is likely that these women would return to the original facility. We did have access to the hospital identification number and adjusted for the correlated nature of the outcome data (nesting by hospital) using this identification number and generalized estimating equations.

LOS is a popular outcome measure in clinical epidemiology. It may be argued, though, that a PLOS is not necessarily a marker for better or worse care. Danel et al[15] conducted a retrospective study of maternal morbidity during labor and delivery and concluded that, "Length of hospital stay after delivery may constitute a measure of severity, but its validity for this purpose must be evaluated." Nonetheless, preeclampsia/eclampsia remains a burden on society and the health care system. In a Dutch cohort of 120 women with a history of early-onset preeclampsia in their first pregnancy, 25% experienced preeclampsia again in their second pregnancy.[16] Furthermore, the patients in our study had a combined length of stay of 22,728 days. Elucidating the clinical epidemiology of this condition may lead to strategies for reducing its morbidity.

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Data analysis and interpretation: Mulla, Nuwayhid
Manuscript draft: Mulla
Statistical expertise: Mulla
Administrative, technical, or material assistance: Gonzalez-Sanchez, Nuwayhid