Hypertension

ORIGINAL ARTICLE

Chronic Hypertension During Pregnancy: Prevalence and Treatment in the United States, 2008–2021

Stephanie A. Leonard, Sara Siadat, Elliott K. Main, Krista F. Huybrechts, Yasser Y. El-Sayed, Mark A. Hlatky, Jheanelle Atkinson, Ayesha Sujan, Brian T. Bateman

BACKGROUND: Treatment of chronic hypertension during pregnancy has been shown to reduce the risk of adverse perinatal outcomes. In this study, we examined the prevalence and treatment of chronic hypertension during pregnancy and assessed changes in these outcomes following the release of the updated 2017 hypertension guidelines of the American College of Cardiology and American Heart Association.

METHODS: We analyzed the Merative™ Marketscan® Research Database of United States commercial insurance claims from 2007 to 2021. We assessed the prevalence of chronic hypertension during pregnancy and oral antihypertensive medication use over time. We then performed interrupted time series analyses to evaluate changes in these outcomes.

RESULTS: The prevalence of chronic hypertension steadily increased from 1.8% to 3.7% among 1 900 196 pregnancies between 2008 and 2021. Antihypertensive medication use among pregnant individuals with chronic hypertension was relatively stable (57%–60%) over the study period. The proportion of pregnant individuals with chronic hypertension treated with methyldopa or hydrochlorothiazide decreased (from 29% to 2% and from 11% to 5%, respectively), while the proportion treated with labetalol or nifedipine increased (from 19% to 42% and from 9% to 17%, respectively). The prevalence or treatment of chronic hypertension during pregnancy did not change following the 2017 American College of Cardiology and American Heart Association hypertension guidelines.

CONCLUSIONS: The prevalence of chronic hypertension during pregnancy doubled between 2008 and 2021 in a nationwide cohort of individuals with commercial insurance. Labetalol replaced methyldopa as the most commonly used antihypertensive during pregnancy. However, only about 60% of individuals with chronic hypertension in pregnancy were treated with antihypertensive medications. ***(Hypertension.* 2024;81:1716–1723. DOI: 10.1161/HYPERTENSIONAHA.124.22731.)**
• **Supplement Material**.

Key Words: antihypertensive agents ■ hypertension ■ interrupted time series analysis ■ labetalol ■ nifedipine ■ methyldopa ■ pregnancy

See Editorial, pp 1724-1727

Chronic hypertension in pregnancy is associated with adverse maternal and fetal/neonatal outcomes, including more than 2-fold increases in the risks of severe maternal morbidity and preterm birth.[1,2] Evidence from randomized controlled trials suggests that medication treatment for mild and moderate chronic hypertension in pregnancy substantially reduces the risk of developing severe hypertension and preeclampsia without having adverse effects on the fetus.[3–5] However, current evidence is limited in regard to clinical practice patterns for pregnant individuals with chronic hypertension.[2]

Correspondence to: Stephanie A. Leonard, Department of Obstetrics and Gynecology, Stanford University School of Medicine, 453 Quarry Rd, MC 5317, Stanford, CA 94305. Email stephanie.leonard@stanford.edu
Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/HYPERTENSIONAHA.124.22731.
For Sources of Funding and Disclosures, see pages 1722 & 1723.

Hypertension is available at www.ahajournals.org/journal/hyp

NOVELTY AND RELEVANCE

What Is New?

We assessed the prevalence and treatment of chronic hypertension during pregnancy before and after the updated 2017 hypertension guidelines of the American College of Cardiology and American Heart Association. The prevalence of chronic hypertension during pregnancy steadily increased, to 3.7% in 2021, but medication treatment was relatively stable (57%–60%). Labetalol replaced methyldopa as the most used medication.

What Is Relevant?

Chronic hypertension during pregnancy confers an increased risk of adverse maternal and fetal/neonatal outcomes. Recently, strong evidence has suggested that medication treatment for mild and moderate chronic hypertension during pregnancy reduces the risk of severe hypertension and preeclampsia.

Clinical/Pathophysiological Implications?

The findings of this study underscore the need to ensure the accuracy of chronic hypertension diagnosis for pregnant individuals and to promote adherence to recent diagnosis and treatment guidelines before pregnancy, which could improve the ability to target blood pressure goals during pregnancy in line with the 2022 American College of Obstetricians and Gynecologists guidelines.

Nonstandard Abbreviations and Acronyms

ACC	American College of Cardiology
ACOG	American College of Obstetricians and Gynecologists
AHA	American Heart Association
ICD-CM	International Classification of Diseases-Clinical Modification

Understanding chronic hypertension diagnosis and treatment patterns during pregnancy is particularly important at this time, as clinical guidelines for chronic hypertension have moved toward diagnosis and treatment at lower blood pressure values.[6–8] In 2017, the American College of Cardiology (ACC) and the American Heart Association (AHA) clinical guidelines revised the thresholds to diagnose hypertension: from 140–159/90–109 to 130–139/80–89 mm Hg for stage 1, and from ≥160/110 to ≥140/90 mm Hg for stage 2.[6] They recommended medication treatment for stage 2 hypertension in nonpregnant adults and for stage 1 hypertension in individuals with diabetes or renal disease.[6] Subsequent publications hypothesized that these revised definitions would increase the number of individuals classified as hypertensive before pregnancy and, correspondingly, increase the number of obstetric patients on antihypertensive therapy.[7,9,10] Researchers in 1 study applied the ACC/AHA guidelines to blood pressure data from pregnant participants in the National Health and Nutrition Examination Survey 2011–2014, and estimated that twice as many reproductive-aged women in the United States would be diagnosed with chronic hypertension based on the new guidelines.[10] However, the actual effect of these guidelines on chronic hypertension during pregnancy has not been evaluated.

Guidelines for the treatment of chronic hypertension during pregnancy have also changed over time. In 2013, the American College of Obstetricians and Gynecologists (ACOG) updated its recommendations for hypertensive disorders in pregnancy and added labetalol and nifedipine to methyldopa as recommended first-line outpatient treatments for chronic hypertension. Then, in 2019, ACOG removed methyldopa from its recommendations, based in large part on a Cochrane Review.[3,7] However, comparative effectiveness studies of methyldopa, labetalol, and nifedipine as antihypertensive medications in pregnancy have not been conclusive.[11–13] Furthermore, prescribing patterns of different antihypertensive medications, including among patients with high-risk comorbidities, have not been assessed in contemporary, large cohorts.

In this study, we examined the prevalence and treatment of chronic hypertension during pregnancy and assessed changes in prevalence and treatment following the release of the updated 2017 ACC/AHA hypertension guidelines.

METHODS

Data Availability

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to Merative™ at https://www.merative.com.

Study Population

We analyzed the Merative™ Marketscan® Research Database of commercial insurance claims for 2007 to 2021.[14] The database includes claims for inpatient and outpatient encounters and outpatient pharmaceutical fills, as well as enrollment data, from large employers and health plans across the United States that provide private health care coverage for employees,

their spouses, and dependents. The claims include a variety of fee-for-service, preferred provider organizations, and capitated health plans.

We applied established methods to identify pregnancies, link live births with infants, and estimate gestational age.[15,16] We defined eligibility for the study as individuals who had pharmaceutical insurance coverage in pregnancy with continuous enrollment from 90 days before the estimated last menstrual period through the date of birth. The Stanford University Research Compliance Office provided ethics approval for this study. We followed the Reporting of Studies Conducted Using Observational Routinely Collected Health Data guidelines for the reporting of this observational cohort study using routinely collected health data.[17]

Chronic Hypertension

Chronic hypertension in pregnancy is defined by ACOG as hypertension diagnosed before pregnancy or before 140 days (20 weeks) of gestation.[7] We used the *International Classification of Diseases-Clinical Modification* (*ICD-CM*), *Ninth* and *Tenth Revisions*, diagnosis codes assigned between 90 days before and 140 days after the estimated last menstrual period to identify cases of primary (essential) hypertension in pregnancy (*ICD-9-CM*: 401, 642.0, 642.7; *ICD-10-CM*: I10, O10.0, O11). Diagnosis codes for chronic hypertension during pregnancy have been found to have high validity, using medical records as the gold standard (sensitivity 88%; specificity 99%; positive predictive value 89%; negative predictive value 99%).[18]

Antihypertensive Medications and Patient Characteristics

We identified oral antihypertensive medications dispensed by outpatient pharmacies using a previously established list of medications (Table S1).[19] We considered an individual to have taken an antihypertensive medication if it was dispensed at least once between the estimated last menstrual period and the date of birth. Individuals could be exposed to >1 medication. If a person received a combination drug (eg, hydrochlorothiazide/labetalol hydrochloride), we classified them as exposed to each component (eg, both hydrochlorothiazide and labetalol hydrochloride).

We assessed patient characteristics, including age, region of residence in the United States, and birth year. We identified conditions that often coexist with chronic hypertension and increase the risk of adverse pregnancy outcomes,[2] including class 3 obesity (body mass index ≥40 kg/m^2), chronic renal disease, diabetes (type 1 or 2), systemic lupus erythematosus, thyroid disorder, and multifetal gestation (which could affect blood pressure and treatment during pregnancy). We used diagnosis codes to identify these conditions (Table S2) and considered them to be present if at least 1 diagnosis code was recorded between 90 days before the last menstrual period and the date of birth.

Statistical Analysis

We first described the characteristics of individuals with and without chronic hypertension and, among those with chronic hypertension, the characteristics of those who were and were not dispensed an antihypertensive medication in pregnancy. Among individuals with chronic hypertension, we calculated the rates of antihypertensive medication use (any and specific medications) stratified by the presence of comorbidities. We plotted the utilization rates of the most commonly dispensed antihypertensive medications by birth year (2008–2021) to assess any changes over time in specific medications.

We conducted interrupted time series analyses to evaluate whether there were changes in (1) the proportion of pregnant individuals diagnosed with chronic hypertension and (2) the use of antihypertensive medications in pregnancy among individuals with chronic hypertension following the release of the ACC/AHA hypertension guidelines in November 2017.[20] For these analyses, we used modified Poisson regression to model the outcomes of births per month that (1) had a prior diagnosis of chronic hypertension and (2) were exposed to an antihypertensive medication during pregnancy. We treated November 2017 as the impact time point, and data from the following 6 months were excluded from analyses (November 2017 to April 2018). We checked all model assumptions, including the autocorrelation of observations, stationarity, and normal distribution of residuals. We replicated the models using generalized linear autoregressive moving average models because minimal autocorrelation was detected.[21]

Sensitivity Analyses

We conducted several sensitivity analyses of antihypertensive medication use. First, we stratified analyses across perinatal time periods: prepregnancy (0–90 days before the date of the last menstrual period), first trimester of pregnancy (last menstrual period through 13 weeks and 6 days of gestation), and second/third trimesters of pregnancy (14 weeks and 0 days of gestation to birth). Treatment patterns during these perinatal periods could potentially differ because of fetal considerations and a known or unknown pregnancy status. For example, lisinopril and losartan are contraindicated in the second and third trimesters.[22] Next, we stratified by patient age (<35 or ≥35 years). Finally, we plotted time trends in antihypertensive medication utilization by region of residence (north central, northeast, south, and west) to explore possible geographic variation in practice patterns.

RESULTS

The prevalence of chronic hypertension among 1 900 196 pregnancies between 2008 and 2021 was 2.7% (n=51 654; Figure S1). A higher proportion of individuals with chronic hypertension were ≥35 years of age, lived in the south, and had comorbidities (Table 1). Among individuals with chronic hypertension, those who used an antihypertensive medication were older and had higher rates of class 3 obesity, diabetes, and chronic renal disease.

Overall, 59% of individuals with chronic hypertension received a medication during the study period (Table 2). Antihypertensive medications were used more often among individuals with class 3 obesity (64%), diabetes (62%), chronic renal disease (67%), or multifetal gestation (63%), and less often among individuals with

Table 1. Patient Characteristics by Chronic Hypertension and Treatment Status

	No chronic hypertension, n=1 848 542	Chronic hypertension, n=51 654	
Characteristics		Antihypertensive medication	
		Yes, n=30 678	No, n=20 976
Birth year			
2008–2017	1 460 537 (79%)	22 392 (73%)	15 476 (74%)
2018–2021	388 005 (21%)	8286 (27%)	5500 (26%)
Age category			
<25 y	99 022 (5.4%)	563 (1.8%)	782 (3.7%)
25–34 y	1 297 132 (70%)	16 640 (54%)	12 999 (62%)
≥35 y	452 388 (24%)	13 475 (44%)	7195 (34%)
Region of the United States			
Northeast	442 240 (24%)	4061 (13%)	4020 (19%)
North central	310 672 (17%)	6200 (20%)	3982 (19%)
South	726 146 (39%)	16 499 (54%)	9997 (48%)
West	350 427 (19%)	3562 (12%)	2743 (13%)
Unknown	19 057 (1.0%)	356 (1.2%)	234 (1.1%)
Class 3 obesity	47 163 (2.6%)	4954 (16%)	2818 (13%)
Diabetes (type 1 or 2)	63 061 (3.4%)	5015 (16%)	3026 (14%)
Chronic renal disease	12 926 (0.7%)	1085 (3.5%)	531 (2.5%)
Systemic lupus erythematosus	4236 (0.2%)	230 (0.7%)	181 (0.9%)
Thyroid disorder	147 632 (8.0%)	4077 (13%)	3208 (15%)
Multifetal gestation	48 390 (2.6%)	1244 (4.1%)	726 (3.5%)

Cells show n (column %).

systemic lupus erythematosus (56%) or thyroid disorder (56%). In the full study population, the most commonly dispensed medications in pregnancy were as follows: labetalol (32% of chronic hypertension patients), methyldopa (17%), nifedipine (11%), and hydrochlorothiazide (8%; Table 2). Differences in patterns of use of different medications by comorbidities were small, with some exceptions. For example, a higher proportion of individuals with class 3 obesity, diabetes, chronic renal disease, or systemic lupus erythematosus received lisinopril and losartan than individuals without these comorbidities. In addition, among individuals who received a medication, a higher proportion of those with systemic lupus erythematosus received nifedipine (26% versus 18% with no comorbidities) and a lower proportion received methyldopa (20% versus 29% with no comorbidities).

Table 2. Patterns of Antihypertensive Medications Dispensed in Pregnancy Among Individuals With Chronic Hypertension by Comorbidity Status

Medications	All	No comorbidities	Class 3 obesity	Diabetes (type 1 or 2)	Chronic renal disease	Systemic lupus erythematosus	Thyroid disorder	Multifetal gestation
	51 654	30 878	7772	8041	1616	411	7285	1970
Any medication	30 678 (59.4%)	18 073 (58.5%)	4954 (63.7%)	5015 (62.4%)	1085 (67.1%)	230 (56.0%)	4077 (56.0%)	1244 (63.1%)
Labetalol	16 602 (32.1%)	9478 (30.7%)	3064 (39.4%)	2686 (33.4%)	621 (38.4%)	117 (28.5%)	2224 (30.5%)	735 (37.3%)
Methyldopa	8702 (16.8%)	5290 (17.1%)	1176 (15.1%)	1515 (18.8%)	265 (16.4%)	46 (11.2%)	1074 (14.7%)	317 (16.1%)
Nifedipine	5721 (11.1%)	3222 (10.4%)	1020 (13.1%)	996 (12.4%)	274 (17.0%)	59 (14.4%)	719 (9.9%)	295 (15.0%)
Hydrochlorothiazide	4134 (8.0%)	2410 (7.8%)	753 (9.7%)	695 (8.6%)	125 (7.7%)	31 (7.5%)	526 (7.2%)	129 (6.5%)
Metoprolol	2606 (5.0%)	1531 (5%)	400 (5.1%)	415 (5.2%)	112 (6.9%)	25 (6.1%)	399 (5.5%)	102 (5.2%)
Amlodipine	2113 (4.1%)	1223 (4%)	361 (4.6%)	384 (4.8%)	105 (6.5%)	18 (4.4%)	261 (3.6%)	55 (2.8%)
Lisinopril	1795 (3.5%)	909 (2.9%)	369 (4.7%)	471 (5.9%)	83 (5.1%)	18 (4.4%)	219 (3.0%)	44 (2.2%)
Atenolol	861 (1.7%)	499 (1.6%)	118 (1.5%)	154 (1.9%)	18 (1.1%)	<11	128 (1.8%)	32 (1.6%)
Losartan	591 (1.1%)	281 (0.9%)	149 (1.9%)	160 (2.0%)	35 (2.2%)	12 (2.9%)	77 (1.1%)	16 (0.8%)
Propranolol	553 (1.1%)	341 (1.1%)	81 (1.0%)	67 (0.8%)	20 (1.2%)	<11	97 (1.3%)	21 (1.1%)
Other	3156 (6.1%)	1834 (5.9%)	467 (6.0%)	617 (7.7%)	159 (9.8%)	35 (8.5%)	410 (5.6%)	81 (4.1%)

Cells display n (column %). Cell sizes <11 not shown per data use agreement to protect confidentiality.

Time Trends

The use of specific antihypertensive medications changed significantly over time: methyldopa use decreased from 29% to 2% and hydrochlorothiazide from 11% to 5%, while the use of labetalol increased from 19% to 42% and the use of nifedipine increased from 9% to 17% (Figure 1). The increase in nifedipine use largely occurred during the latter half of the study period.

The prevalence of chronic hypertension during pregnancy steadily increased from 1.8% in 2008 to 3.7% in 2021. In the interrupted time series analysis, we found no change in the slope of this trend following the release of the ACC/AHA hypertension guidelines (slope change relative risk, 1.00 [95% CI, 1.00–1.00]; P=0.20); however, there was a statistically significant 8% decrease in chronic hypertension prevalence following the 6 months after the ACC/AHA guidelines release (level change relative risk, 0.92 [95% CI, 0.87–0.96]; P<0.001; Figure 2).

During the same period of time, 2008 to 2021, the use of an antihypertensive medication during pregnancy among individuals with chronic hypertension increased slightly, from 58% to 60% (Figure 3). In the interrupted time series analysis, we found no slope or level changes in this trend following the ACC/AHA hypertension guidelines in 2017 (slope change relative risk, 1.00 [95% CI, 1.00–1.00]; P=0.58; level change relative risk, 1.01 [95% CI, 0.98–1.04]; P=0.69).

In sensitivity analyses, we found the use of antihypertensive medications was 43% before pregnancy, 49% in the first trimester, and 52% in the second or third trimester (Table S3). The use of lisinopril and losartan before pregnancy and in the first trimester was highest (1.9%–9.3%) among individuals with comorbid class 3 obesity, diabetes, chronic renal disease, or systematic lupus erythematosus, and then decreased to 0.1% to 0.4% in the second/third trimesters. In all 3 perinatal periods, the use of methyldopa and hydrochlorothiazide decreased, and the use of labetalol and nifedipine increased over time (Figure S2). The magnitude of the absolute changes over time was larger in the second and third trimesters. In analyses stratified by age, antihypertensive medication use was higher in individuals with chronic hypertension who were ≥35 years old than those <35 years old (65% versus 56%; Table S4). Minimal differences existed between the 2 age groups in the trends of specific medication utilization rates over time (Figure S3). Finally, we assessed whether time trends in medication use varied by region of the United States, finding the lowest utilization rates of any antihypertensive medication in the northeast (in 2020–2021: 52% in the northeast, 56% in the west, 61% in the north central, and 62% in the south; Figure S4). Methyldopa had the highest utilization rate of all medications from 2008 to 2011 in the south, but not in other regions. By 2021, the comparative utilization rates of methyldopa, labetalol, and nifedipine were similar across regions.

DISCUSSION

This study of ≈2 million pregnancies across the United States between 2008 and 2021 found that the prevalence of chronic hypertension doubled (from 1.8% to 3.7%). The prevalence of chronic hypertension rose steadily over the study period, without a significant alteration following the release of the 2017 ACC/AHA hypertension guidelines. The use of antihypertensive medications increased only slightly between 2008 and 2021, with ≈60% of pregnant individuals with chronic hypertension receiving an oral antihypertensive medication. The types of antihypertensive medications used, however, changed dramatically over time, with a precipitous drop in the use of methyldopa and a substantial increase in the use of labetalol (Figure 1).

The increase in chronic hypertension during pregnancy over the 14-year study period was substantial, but it cannot be attributed to the change in diagnostic

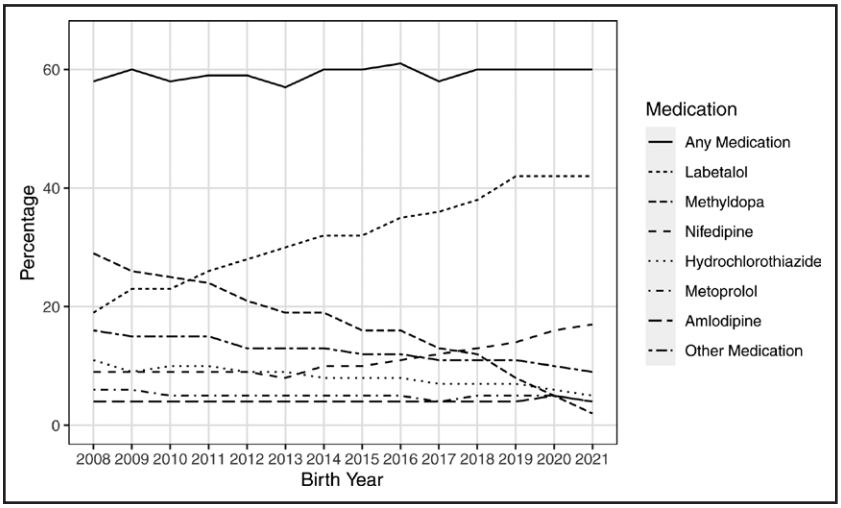

Figure 1. Trend of antihypertensive medication use in pregnancy over time among patients with chronic hypertension.

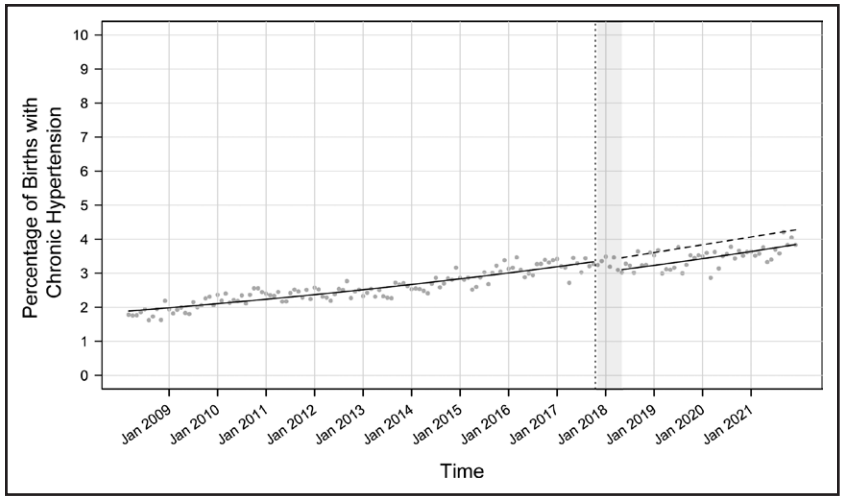

Figure 2. Results of interrupted time series analysis evaluating changes in the prevalence of chronic hypertension in pregnancy following the release of the American College of Cardiology and American Heart Association (ACC/AHA) hypertension guidelines in November 2017.
Circles represent the observed average percentage among births in a given month. The solid-fitted line is the best fit line before and after the ACC/AHA guidelines from the analytical model. The dashed-fitted line is the predicted best fit line based on the observations before the ACC/AHA guidelines.

criteria for hypertension promulgated in the 2017 ACC/AHA hypertension guidelines. This finding was contrary to prior expectations that the updated guidelines would greatly increase the prevalence of chronic hypertension diagnosed before pregnancy[7,10,23] and thus increase the use of antihypertensive medications during pregnancy. The steady increase in hypertension is consistent with trends observed in earlier time periods[2,24] as well as trends in the general United States adult population.[23] A prior analysis of national data from 1970 to 2010 suggests that the increasing trend in chronic hypertension during pregnancy is attributable in part to increasing maternal age.[24] Other factors, such as increased vigilance in diagnosis and coding, could potentially contribute to the trend as well.

Our study further found little change in the proportion of individuals with chronic hypertension during pregnancy treated with an antihypertensive medication, which remained around 60% during the study period. This finding was also similar to trends reported for other United States adult populations, including reproductive-aged adults.[25,26] Among adults aged 20 to 44 years, nationally representative estimates of antihypertensive treatment rates from the National Health and Nutrition Examination Survey were around 60% in both 2009–2010 and 2017–2020 survey waves.[25] Together, these findings suggest that the 2017 ACC/AHA hypertension guidelines did not affect hypertension diagnosis and treatment rates in the United States, and these rates may be lowest among younger, reproductive-aged individuals.

The small change in use of antihypertensive medications found in our study may also be due, in part, to the controversy during the study period about the benefits and harms of antihypertensive treatment of mild hypertension in pregnancy.[7,27,28] ACOG did not recommend antihypertensive treatment of mild hypertension in pregnancy (blood pressure <160 mm Hg systolic or 105 mm Hg diastolic) until 2022.[8] The updated recommendation followed the publication of a large randomized controlled trial, which showed a substantial improvement in maternal and neonatal outcomes from a strategy of reducing blood pressure to <140/90 mm Hg in pregnancy.[4] These revised guidelines may increase medication treatment for chronic hypertension in pregnancy, and future evaluation of this potential effect will be important.

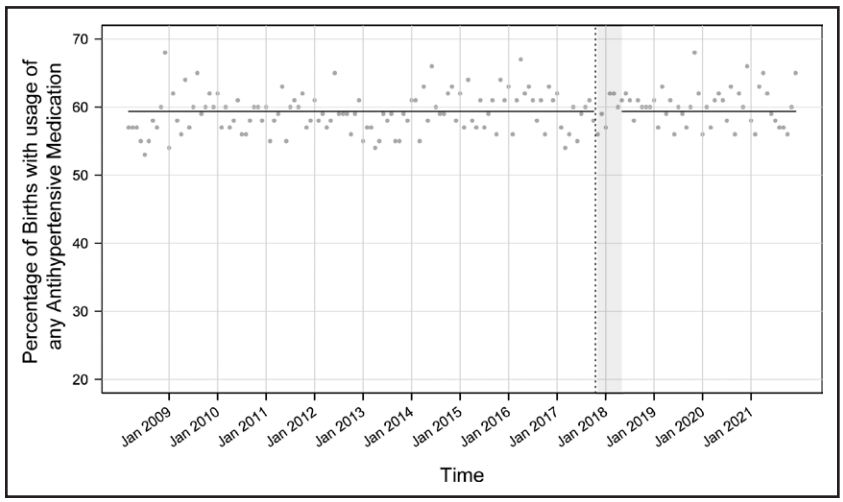

Figure 3. Results of interrupted time series analysis evaluating changes in the medication treatment rate for pregnant individuals with chronic hypertension following the release of the American College of Cardiology and American Heart Association (ACC/AHA) hypertension guidelines in November 2017.
Circles represent observed average percentage among births in a given month. The solid-fitted line is the best fit line before and after the ACC/AHA guidelines from the analytical model, and it overlays a dashed-fitted line that is the predicted best fit line based on the observations before the ACC/AHA guidelines.

We found clear changes between 2008 and 2021 in the types of antihypertensive medications prescribed to pregnant individuals with chronic hypertension. These changes may have occurred in response to revised clinical recommendations, new data on effectiveness and safety, wider clinical experience with available medications, and changes in medications available at pharmacies.[27–29] For decades, methyldopa, an alpha-agonist, was the preferred first-line therapy because of its long history of safe use in pregnancy.[27,30] In 2000, ACOG clinical guidelines in the United States were released that, for the first time, stated that labetalol, a combined α- and β-blocker, could be used as an alternative to methyldopa for the treatment of chronic hypertension in pregnancy.[27] The ACOG guidelines were next updated in 2013, for the first time recommending nifedipine, a calcium-channel blocker, in addition to labetalol and methyldopa as options for antihypertensive treatment in pregnancy.[28] These changes in guidelines could have influenced prescribing patterns, as the increasing trend in labetalol use likely began as far back as 2000,[31] and our results showed nifedipine use to gradually increase after 2013. ACOG, however, continued to recommend methyldopa as a first-line antihypertensive medication until 2019, when a Cochrane Review reported that beta-blockers and calcium-channel blockers were more effective than methyldopa in reducing the risk of severe hypertension in pregnancy, with no differences in preeclampsia or fetal/neonatal outcomes.[3,7] Our study of national data in the United States shows that use of methyldopa dropped dramatically, yet steadily, over the period of 2008 to 2021. This downward trend could potentially be accelerated since 2021 with the discontinuation of methyldopa production by pharmaceutical companies.[29]

The use of antihypertensive medication during pregnancy was modestly higher in individuals with a comorbidity (61%) than in those without a comorbidity (59%). Medication use was particularly high in individuals with chronic renal disease (67%) and class 3 obesity (64%), which are 4× to 6× more common in pregnant individuals with chronic hypertension.[2] The combination of chronic hypertension with chronic renal disease, diabetes, or systemic lupus erythematosus has been found to have particularly strong associations with adverse maternal and fetal outcomes.[2]

This study has several important limitations. The database we analyzed contained information on medications that were dispensed, but we do not know whether an individual was adherent to the prescribed regimen. We did not have information on the stage of hypertension or blood pressure measurements to assess the severity of the disease, nor could we assess the extent to which specific blood pressure levels used to diagnose chronic hypertension may have changed over time. Although we restricted the study to individuals with chronic hypertension, the antihypertensive medications could have been prescribed for other indications, such as the use of nifedipine as a tocolytic agent. However, this practice is typically done inpatient, and our study was restricted to outpatient medication fills. The data set contained limited sociodemographic data, and we were therefore limited in assessing differences in treatment patterns by patient characteristics. The study used claims data from beneficiaries of commercial health insurance programs, and the generalizability of our results to individuals with Medicaid or other sources of payment is not known. In addition, the generalizability of the results to other countries is unknown; as of 2022, several international clinical practice guidelines continue to recommend methyldopa and do not recommend nifedipine as first-line agents for nonsevere hypertension in pregnancy.[32]

PERSPECTIVES

We found that the prevalence of chronic hypertension doubled among pregnant individuals between 2008 and 2021 in a national commercial claims database in the United States. The use of an antihypertensive medication to treat chronic hypertension during pregnancy remained between 57% and 60% over the 14-year study period. The proportion of pregnant individuals diagnosed with chronic hypertension or treated with antihypertensive medication during pregnancy did not change following the release of the updated 2017 ACC/AHA hypertension guidelines. There were large shifts in the medications used to treat chronic hypertension in pregnancy, with labetalol supplanting methyldopa as the most commonly used antihypertensive medication. These findings underscore the need to ensure the accuracy of chronic hypertension diagnosis for pregnant individuals and to promote adherence to recent diagnosis and treatment guidelines before pregnancy, which could improve the ability to target blood pressure goals during pregnancy in line with the 2022 ACOG guidelines.

ARTICLE INFORMATION

Received January 10, 2024; accepted April 3, 2024.

Affiliations

Department of Obstetrics and Gynecology (S.A.L., E.K.M., Y.Y.E.-S.), Department of Anesthesiology, Perioperative and Pain Medicine (S.S., A.S., B.T.B.), Departments of Health Policy and Medicine (M.A.H.), Stanford University School of Medicine, CA. Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA (K.F.H.). Meharry Medical College, Nashville, TN (J.A.).

Acknowledgments

Data for this project were accessed using the Stanford Center for Population Health Sciences Data Core.

Sources of Funding

Funding for this work was provided in part by the National Heart, Lung, and Blood Institute (K01HL171699 to S.A. Leonard and R01HL139844 to M.A. Hlatky) and National Center for Advancing Translational Science Clinical and

Translational Science Award (UL1TR003142 to the Stanford Center for Population Health Sciences Data Core). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Disclosures

K.F. Huybrechts reports being an investigator on grants to Brigham and Women's Hospital from Takeda and UCB for unrelated work.

Supplemental Material

Figures S1–S4
Tables S1–S4

REFERENCES

1. Leonard SA, Formanowski BL, Phibbs CS, Lorch S, Main EK, Kozhimannil KB, Passarella M, Bateman BT. Chronic hypertension in pregnancy and racial–ethnic disparities in complications. *Obstet Gynecol*. 2023;142:862–871. doi: 10.1097/AOG.0000000000005342
2. Bateman BT, Bansil P, Hernandez-Diaz S, Mhyre JM, Callaghan WM, Kuklina EV. Prevalence, trends, and outcomes of chronic hypertension: a nationwide sample of delivery admissions. *Am J Obstet Gynecol*. 2012;206:134.e1–134.e8. doi: 10.1016/j.ajog.2011.10.878
3. Abalos E, Duley L, Steyn DW, Gialdini C. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. *Cochrane Database Syst Rev*. 2018;10:CD002252. doi: 10.1002/14651858.CD002252.pub4
4. Tita AT, Szychowski JM, Boggess K, Dugoff L, Sibai B, Lawrence K, Hughes BL, Bell J, Aagaard K, Edwards RK, et al; Chronic Hypertension and Pregnancy (CHAP) Trial Consortium. Treatment for mild chronic hypertension during pregnancy. *N Engl J Med*. 2022;386:1781–1792. doi: 10.1056/NEJMoa2201295
5. Magee LA, von Dadelszen P, Rey E, Ross S, Asztalos E, Murphy KE, Menzies J, Sanchez J, Singer J, Gafni A, et al. Less-tight versus tight control of hypertension in pregnancy. *N Engl J Med*. 2015;372:407–417. doi: 10.1056/NEJMoa1404595
6. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines hypertension. *Hypertension*. 2018;71:1269–1324. doi: 10.1161/HYP.0000000000000066
7. ACOG. ACOG practice bulletin no. 203: chronic hypertension in pregnancy. *Obstet Gynecol*. 2019;133:e26. doi: 10.1097/AOG.0000000000003020
8. ACOG. Clinical guidance for the integration of the findings of the Chronic Hypertension and Pregnancy (CHAP) Study. 2022. Accessed December 6, 2022. https://www.acog.org/en/clinical/clinical-guidance/practice-advisory/articles/2022/04/clinical-guidance-for-the-integration-of-the-findings-of-the-chronic-hypertension-and-pregnancy-chap-study
9. Battarbee AN, Sinkey RG, Harper LM, Oparil S, Tita ATN. Chronic hypertension in pregnancy. *Am J Obstet Gynecol*. 2020;222:532–541. doi: 10.1016/j.ajog.2019.11.1243
10. Topel ML, Duncan EM, Krishnal, Badell ML, Vaccarino V, Quyyumi AA. Estimated impact of the 2017 American College of Cardiology/American Heart Association blood pressure guidelines on reproductive-aged women. *Hypertension*. 2018;72:e39–e42. doi: 10.1161/HYPERTENSIONAHA.118.11660
11. Bone JN, Sandhu A, Abalos ED, Khalil A, Singer J, Prasad S, Omar S, Vidler M, von Dadelszen P, Magee LA. Oral antihypertensives for nonsevere pregnancy hypertension: systematic review, network meta- and trial sequential analyses. *Hypertension*. 2022;79:614–628. doi: 10.1161/HYPERTENSIONAHA.121.18415
12. Magee L, von Dadelszen P, Singer J, Lee T, Rey E, Ross S, Asztalos E, Murphy KE, Menzies J, Sanchez J, et al; CHIPS Study Group. Do labetalol and methyldopa have different effects on pregnancy outcome? Analysis of data from the Control of Hypertension In Pregnancy Study (CHIPS) trial. *BJOG*. 2016;123:1143–1151. doi: 10.1111/1471-0528.13569
13. Dublin S, Idu A, Avalos LA, Cheetham TC, Easterling TR, Chen L, Holt VL, Nance N, Bider-Canfield Z, Neugebauer RS, et al. Maternal and neonatal outcomes of antihypertensive treatment in pregnancy: a retrospective cohort study. *PLoS One*. 2022;17:e0268284. doi: 10.1371/journal.pone.0268284
14. Stanford Center for Population Health Sciences. Marketscan Databases. https://doi.org/10.57761/kg3j-nh50
15. MacDonald SC, Cohen JM, Panchaud A, McElrath TF, Huybrechts KF, Hernandez-Diaz S. Identifying pregnancies in insurance claims data: Methods and application to retinoid teratogenic surveillance. *Pharmacoepidemiol Drug Saf*. 2019;28:1211–1221. doi: 10.1002/pds.4794
16. Ailes EC, Zhu W, Clark EA, Huang YA, Lampe MA, Kourtis AP, Reefhuis J, Hoover KW. Identification of pregnancies and their outcomes in healthcare claims data, 2008–2019: an algorithm. *PLoS One*. 2023;18:e0284893. doi: 10.1371/journal.pone.0284893
17. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM; RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Med*. 2015;12:e1001885. doi: 10.1371/journal.pmed.1001885
18. Labgold K, Stanhope KK, Joseph NT, Platner M, Jamieson DJ, Boulet SL. Validation of hypertensive disorders during pregnancy: ICD-10 codes in a high-burden southeastern United States hospital. *Epidemiology*. 2021;32:591–597. doi: 10.1097/EDE.0000000000001343
19. Bateman BT, Huybrechts KF, Fischer MA, Seely EW, Ecker JL, Oberg AS, Franklin JM, Mogun H, Hernandez-Diaz S. Chronic hypertension in pregnancy and the risk of congenital malformations: a cohort study. *Am J Obstet Gynecol*. 2015;212:337.e1–337.14. doi: 10.1016/j.ajog.2014.09.031
20. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol*. 2017;46:348–355. doi: 10.1093/ije/dyw098
21. Dunsmuir WTM. Generalized linear autoregressive moving average models. In: *Handbook of Discrete-Valued Time Series, Handbooks of Modern Statistical Methods*. CRC Press; 2015. Accessed September 15, 2023. https://www.routledgehandbooks.com/doi/10.1201/b19485-5
22. Bateman BT, Patorno E, Desai RJ, Seely EW, Mogun H, Dejene SZ, Fischer MA, Friedman AM, Hernandez-Diaz S, Huybrechts KF. Angiotensin-converting enzyme inhibitors and the risk of congenital malformations. *Obstet Gynecol*. 2017;129:174–184. doi: 10.1097/AOG.0000000000001775
23. Dorans KS, Mills KT, Liu Y, He J. Trends in prevalence and control of hypertension according to the 2017 American College of Cardiology/American Heart Association (ACC/AHA) guideline. *J Am Heart Assoc*. 8888;7:e00. doi: 10.1161/JAHA.118.008888
24. Ananth CV, Duzyj CM, Yadava S, Schwebel M, Tita ATN, Joseph KS. Changes in the prevalence of chronic hypertension in pregnancy, United States, 1970 to 2010. *Hypertension*. 2019;74:1089–1095. doi: 10.1161/HYPERTENSIONAHA.119.12968
25. Aggarwal R, Yeh RW, Joynt Maddox KE, Wadhera RK. Cardiovascular risk factor prevalence, treatment, and control in US adults aged 20 to 44 years, 2009 to March 2020. *JAMA*. 2023;329:899–909. doi: 10.1001/jama.2023.2307
26. Egan BM, Myftari K. Trends in hypertension control among United States adults: is NHANES the outlier? *Hypertension*. 2023;80:2544–2546. doi: 10.1161/HYPERTENSIONAHA.123.21996
27. Report of the national high blood pressure education program working group on high blood pressure in pregnancy. *Am J Obstet Gynecol*. 2000;183:s1–s22. doi: 10.1067/mob.2000.107928
28. Hypertension in pregnancy: executive summary. *Obstet Gynecol*. 2013;122:1122. doi: 10.1097/01.AOG.0000437382.03963.88
29. Drug shortage detail: methyldopa tablets. Accessed March 5, 2024. https://www.ashp.org/Drug-Shortages/Current-Shortages/Drug-Shortage-Detail.aspx?id=462
30. National high blood pressure education program working group report on high blood pressure in pregnancy. *Am J Obstet Gynecol*. 1990;163(5, Part 1):1691–1712. doi: 10.1016/0002-9378(90)90653-O
31. Bateman BT, Hernandez-Diaz S, Huybrechts KF, Palmsten K, Mogun H, Ecker JL, Fischer MA. Patterns of outpatient antihypertensive medication use during pregnancy in a medicaid population. *Hypertension*. 2012;60:913–920. doi: 10.1161/HYPERTENSIONAHA.112.197095
32. Scott G, Gillon TE, Pels A, von Dadelszen P, Magee LA. Guidelines–similarities and dissimilarities: a systematic review of international clinical practice guidelines for pregnancy hypertension. *Am J Obstet Gynecol*. 2022;226(2, Supplement):S1222–S1236. doi: 10.1016/j.ajog.2020.08.018