

Retrospective Study

Association of Gestational Hypertension and Eclampsia to Maternal Smoking by Pre-Pregnancy Body Mass Index Status Among Aged 20-29-Years in the United States

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ABSTRACT

Objective

To investigate whether gestational hypertension (GH) and/or eclampsia was associated with the timing of maternal smoking when stratified by pre-pregnancy body mass index (pBMI) status.

Study Design and Methods

1,376,271 US-born mothers aged 20-29 from the 2019 infant natality data who had a singleton birth (20+ weeks of gestation) were analyzed in this study. Maternal smoking status was defined into five groups, i.e., non-smokers, quit smoking before pregnancy, quit smoking before the 2nd trimester, quit smoking before the 3rd trimester, and smoked whole-time. Odds ratios (ORs) of GH or eclampsia were estimated separately using multiple logistic regression for maternal smoking by pBMI status (kg/m²): underweight (<18.5), normal (18.5≤25.0), overweight (25.0≤30.0), and obese (≥30.0).

Results

Compared to non-smokers, the adjusted ORs (95% CIs) of GH for mothers who quit before pregnancy with pBMI underweight, normal, overweight, and obese were 1.17 (0.92-1.49), 1.11 (1.03-1.19), 1.13 (1.05-1.22), 1.13 (1.08-1.19), respectively. While the ORs (95% CIs) of GH for mothers who smoked for the entirety of their pregnancy were 0.71 (0.60-0.84), 0.80 (0.75-0.84), 0.79 (0.74-0.84), and 0.82 (0.78-0.85), respectively. The adjusted ORs for eclampsia showed a different pattern, only that for mothers who smoked for their whole pregnancy with normal and obese showed significantly (0.69 (0.53-0.91) for normal weight, 0.73 (0.58-0.92) for obese).

Conclusion

In comparison to non-smokers, an increase in the odds of GH were observed amongst normal, overweight, and obese mothers quitting before pregnancy meanwhile a decreased odds were observed amongst mothers smoking throughout pregnancy in all pBMI classes.

Keywords

Maternal smoking; Gestational hypertension; Eclampsia; BMI.

INTRODUCTION

Smoking during pregnancy has been associated with an increased risk of poor outcomes for mother and child such as ectopic pregnancy, placental abruption, preterm birth, low birth weight, and infant mortality.^{1,2} Despite these risks, only half of smokers quit during their pregnancy.³ In the United States, 7.2% of mothers who gave birth in 2016 reported being a smoker, and between 2010 and 2017 smoking prevalence during pregnancy in

the United States (U.S.) was highest in the 20-24 age range followed by ages 15-19 and 25-29.⁴

A US-based study found that certain population subgroups are more likely to smoke during pregnancy and have the lowest prevalence's of quitting during pregnancy.⁵ These subgroups being women who are covered by Medicaid, underweight before pregnancy, high school educated or less, and/or under the age of 25.5 prior research indicates that women who were most

likely to quit smoking during pregnancy were younger than 20, Asian/Pacific Islander, had more than 12-years of education, lived in an urban area, and had private insurance.^{4,5}

Women are more likely to use smoking as a method of weight control and studies have observed that on average smokers have a lower body mass index (BMI) than non-smokers.⁶ Other research has shown smoking as a risk factor for high blood pressure in women however, its effect during pregnancy is unclear.²

In the past twenty years the incidence of hypertensive disorders of pregnancy (HDP) have increased by 25%, and about 5% to 10% of pregnant women are diagnosed with at least one HDP.⁷ This increase in HDP has been attributed to the rise of mothers of an advanced maternal age, obesity, and comorbidities such as diabetes mellitus and nutrient deficiencies.^{2,7} The two most common HDP are gestational hypertension (GH) and pre-eclampsia (PE) with 25 to 50% of those with GH developing PE.^{8,9} GH can only be diagnosed after 20-weeks of gestation.¹⁰ HDP are associated with maternal morbidity and mortality, largely due to maternal strokes.⁷ PE can progress to eclampsia which can be lethal and has an estimated 1.8% mortality rate in developed countries.¹¹

Contradictory results have been found on the impact of smoking during pregnancy on HDP. Studies from Japan and Poland suggested increase in risk while American studies found decrease in risk when smoking during pregnancy.¹²⁻¹⁵ Focusing on the American studies, recent research saw that mothers who were overweight, obese, diagnosed with pre-pregnancy diabetes or with gestational diabetes had notably higher incidences of GH/PE.¹⁵ Additionally, Coghill et al¹⁶ identified that diabetes, which is strongly associated with BMI, was a risk factor for eclampsia. Currently, no studies have explored how maternal smoking is associated with HDP when accounting for weight status.

Research Aim and Hypothesis

This research aims to contribute a focused insight into the risk of GH and eclampsia for US mothers aged 20-29 who smoke, or cease to, during pregnancy while accounting for BMI. It is hypothesized that the protective action of smoking seen in previous studies may be explained by differences in BMI with underweight mothers being more likely to smoke but also less likely to experience HDP.

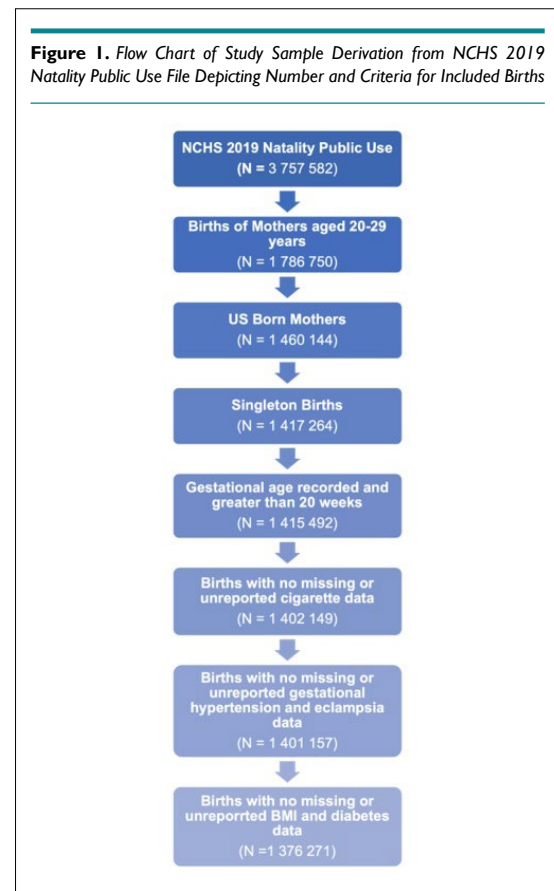
METHODS

Sampling Strategy

The study population is derived from the 2019 National Center for Health Statistics (NCHS) natality data file which includes all live births to US residents in 2019. This file was created using information from the US Standard Certificate of Live Birth and includes 3,757,582 births.¹⁷

The following inclusions and exclusions were made to form the study sample (Figure 1).

Figure 1. Flow Chart of Study Sample Derivation from NCHS 2019 Natality Public Use File Depicting Number and Criteria for Included Births



Only mothers aged 20-29, who were born in the US and had a singleton birth over the gestational age of 20-weeks were included. Mothers aged 20-29-years were selected as previous research has shown that smoking prevalence during pregnancy in the US was highest in the 20-24 age range.⁴ Additionally, those with missing or unreported smoking, BMI, diabetes, GH, and eclampsia were excluded. The resulting sample included 1,376,271 singleton births.

Exposures, Outcomes and Covariates

Smoking was reported as the daily average number of cigarettes smoked three months before pregnancy and during each trimester. Maternal smoking was recategorized into the following groups for analysis: (a) non-smokers (b) smoked before but not during pregnancy (c) smoked before pregnancy and during 1st trimester only (d) smoked before pregnancy and during 1st and 2nd trimester only (e) smoked before pregnancy and all trimesters. Pre-pregnancy BMI (pBMI) data was recategorized into the following four categories: (a) underweight (<18.5kg/m²) (b) normal (18.5≤25.0 kg/m²) (c) overweight (25.0≤30.0 kg/m²) and (d) obese BMI≥30.0 kg/m².

On the birth certificate, GH and eclampsia diagnoses were reported independently. The variable of GH on certificate data includes both pregnancy-induced hypertension and PE.

Potential confounders used in adjustments were categorized as either mother's characteristics or child's characteristics. Those of the mother included: maternal age (years.), maternal race

(white, black, or other), mother's education (less than high school, high school, some college, associate's degree, bachelor's degree, graduate school or unknown), pre-pregnancy diabetes and gestational diabetes. Child's characteristics included: gestational age at birth (weeks), infant sex (female *v.s.* male), and birthweight (very low (227-1499 grams), low (1500-2499 grams), normal (2500-8165 grams) or unknown).

Statistical Analysis

ORs (95% CI) were estimated using logistic regression for either GH or eclampsia by smoking status. To control for confounding, models were stratified by BMI class and conducted three times to

either adjust for mother's characteristics only, child's characteristics only or both. A binary logistic regression model with a significance level of 0.05 was used. All analyses were performed in SAS/STAT software (Studio v3.8, SAS Institute Inc., Cary, NC, USA).¹⁸

RESULTS

Table 1 presents the maternal, pregnancy and neonatal characteristics of the 1,376,271 women included in the study. 8.2% of women GH, and 0.3% had eclampsia. Overall, 11.4% of women smoked before pregnancy, 8.6% during first semester, 7.3% during the second semester, and 6.9% during the third semester. Notably underweight mothers had higher prevalence of smoking before and

Table 1. Demographic Characteristics, Smoking Status, Diabetes Diagnosis and Hypertensive Outcomes of Mothers by BMI Categories

	Underweight* (n=46,384)	Normal* (n=529,002)	Overweight* (n=356,430)	Obese* (n=444,455)
Mother's Demographic Characteristics				
Age (Years), Mean [SD]	24.23 [2.84]	25.05 [2.84]	25.5 [2.77]	25.18 [2.71]
Race (%)				
White	75.73	79.25	76.94	72.83
Black	21.31	17.62	19.73	23.97
Other	2.96	3.13	3.33	3.20
Education (%)				
Less than high school	14.27	9.48	9.09	10.10
Highschool	41.21	32.32	34.21	38.62
Some college	24.39	24.64	26.84	28.53
Associates Degree	6.33	8.69	9.52	9.10
Bachelor's degree	10.30	18.45	15.27	10.43
Graduate School	2.72	5.64	4.28	2.49
Unknown	0.78	0.79	0.80	0.73
Characteristics of this Pregnancy				
<i>Interval Since Last Birth (%)</i>				
No previous births	38.90	40.13	36.88	32.79
4-11-months	3.20	3.39	3.60	3.78
12-23-months	17.82	17.51	17.84	18.51
24-71-months	26.78	25.91	27.04	28.98
≥ 72-months	3.84	4.33	5.41	6.23
Unknown	9.47	8.73	9.23	9.72
Infertility Treatment Used (%)	0.34	0.53	0.55	0.61
Previous Pre-term Birth (%)	4.29	3.12	3.13	3.62
<i>Delivery Type (%)</i>				
Spontaneous	78.38	76.47	71.12	61.19
Forceps	0.61	0.60	0.53	0.40
Vacuum	3.63	3.05	2.53	1.95
Caesarean	17.35	19.85	25.79	36.43
Unknown	0.04	0.03	0.03	0.03
<i>Payment Method (%)</i>				
Medicaid	59.21	45.86	48.63	55.72
Private Insurance	33.36	45.59	43.84	38.63
Self-Pay	3.06	3.27	2.30	1.63
Indian Health Service	0.05	0.08	0.11	0.13
CHAMPUS/TRICARE	1.38	2.10	2.03	1.25
Other Government (Federal, State, Local)	0.88	0.93	1.03	0.96
Other	1.27	1.39	1.33	1.09

Unknown	0.78	0.78	0.74	0.58
Neonatal Characteristics				
Gestational Age, Mean [SD]	38.52 [2.37]	38.81 [2.15]	38.82 [2.13]	38.73 [2.22]
Birthweight (%)				
Very Low (227 - 1499 grams)	0.93	0.60	0.60	0.76
Low (1500 – 2499 grams)	11.48	6.16	5.02	5.15
Normal (2500 - 8165 grams)	87.56	93.21	94.36	94.06
Unknown/not stated	0.04	0.03	0.02	0.02
Sex of the Child (%)				
Female	48.83	48.90	48.78	48.90
Mothers Smoking Status				
Smoked in 3 months before pregnancy (%)	18.78	11.33	10.63	11.34
Smoked in first trimester (%)	15.19	8.71	7.87	8.31
Smoked in second trimester (%)	13.36	7.50	6.67	7.00
Smoked in third trimester (%)	12.72	7.13	6.31	6.61
Mother's Diabetes Status				
Pre-Pregnancy Diabetes (%)	0.26	0.39	0.68	1.35
Gestational Diabetes (%)	2.31	2.48	4.15	8.28
Hypertensive Disorders of Pregnancy				
Gestational Hypertension (%)	3.92	5.22	7.85	12.33
Eclampsia (%)	0.18	0.19	0.27	0.38
*Underweight: BMI<18.5kg/m ² , Normal: BMI 18.5≤25.0 kg/m ² , Overweight: BMI 25.0≤30.0 kg/m ² , Obese: BMI ≥30.0 kg/m ²				

Table 2. Prevalence of Pre-Pregnancy and Gestational Diabetes by Smoking Status and Maternal Pre-Pregnancy Bmi Category

	Non-Smoker	Quit before Pregnancy	Quit after First Trimester	Quit after Second Trimester	Smoked throughout Pregnancy
Pre-pregnancy diabetes (%)					
Underweight	0.26	0.35	0.11	0.00	0.26
Normal	0.38	0.51	0.44	0.61	0.38
Overweight	0.67	0.85	0.66	0.70	0.79
Obese	1.33	1.59	1.52	1.58	1.57
Gestational diabetes (%)					
Underweight	2.20	2.56	2.36	3.93	2.87
Normal	2.46	3.14	2.91	2.28	2.53
Overweight	4.11	4.96	5.11	5.08	4.06
Obese	8.14	10.87	10.24	9.23	8.46
Pre-pregnancy or gestational diabetes (%)					
Underweight	2.46	2.91	2.47	3.93	3.13
Normal	2.84	3.65	3.35	2.89	2.90
Overweight	4.78	5.81	5.77	5.78	4.85
Obese	9.47	12.45	11.76	10.81	10.02

during pregnancy compared to the other BMI categories (smoked before but not during pregnancy: 18.8%, smoked before pregnancy and during 1st trimester only: 15.2%, smoked before pregnancy and during 1st and 2nd trimester only: 13.4%, smoked before pregnancy and all trimesters: 12.7%). 0.8% of women had pre-pregnancy diabetes and 4.8% had gestational diabetes. Pre-pregnancy diabetes and gestational diabetes increased with increasing BMI class regardless of smoking status (Table 2).

Table 3 presents the ORs and confidence intervals for GH by smoking status and pBMI class for each adjustment model

of mother's characteristics, child's characteristics, and both mother and child characteristics. Regardless of adjustment and BMI status, the odds of developing GH for mothers who quit smoking in the three-months before pregnancy were significantly higher in comparison to non-smokers (adjusted OR_{Underweight}=1.17 with 95% CI: 0.92-1.49; adjusted OR_{normal}=1.11 with 95% CI: 1.03-1.19; adjusted OR_{Overweight}=1.13 with 95% CI: 1.05-1.22; adjusted OR_{Obese}=1.13 with 95% CI: 1.08-1.19). Meanwhile, the odds of developing GH were significantly lower for mothers who smoked throughout pregnancy compared to non-smokers in each adjustment model and subsequent BMI category (adjusted OR_{Underweight}

weight=0.71 with 95% CI: 0.60-0.84; adjusted ORnormal=0.80 with 95% CI: 0.75-0.84; adjusted ORoverweight=0.79 with 95% CI: 0.74-0.84; adjusted ORobese=0.82 with 95% CI: 0.78-0.85).

The adjusted ORs for eclampsia showed a different pattern and are shown in Table 4. In comparison to non-smokers, normal and obese women who smoked throughout pregnancy

present a significant decrease in odds of eclampsia when including both mother and child characteristics (adjusted ORnormal=0.69 with 95% CI: 0.53-0.91; adjusted ORobese=0.73 with 95% CI: 0.58-0.92). The odds of eclampsia by smoking status were insignificant for the underweight and overweight BMI groups (adjusted ORunderweight=1.265 with 95% CI: 0.665-2.406; adjusted ORoverweight=1.025 with 95% CI: 0.781-1.345).

Table 3. Adjusted Odds Ratios and Confidence Intervals of Gestational Hypertension by Maternal Pre-pregnancy BMI Category and Smoking Status in Comparison to Non-smokers

	Quit before Pregnancy	Quit after First Trimester	Quit after Second Trimester	Smoked throughout Pregnancy
Adjusting for Mother's Characteristics*				
Underweight	1.154 [0.912-1.462]	1.188 [0.860-1.641]	1.623 [1.059-2.488]	0.808 [0.683-0.956]
Normal	1.092 [1.015-1.175]	1.007 [0.902-1.126]	1.184 [1.004-1.395]	0.913 [0.865-0.963]
Overweight	1.103 [1.027-1.186]	1.065 [0.954-1.190]	0.883 [0.728-1.070]	0.853 [0.804-0.905]
Obese	1.107 [1.053-1.164]	1.039 [0.962-1.122]	1.067 [0.942-1.209]	0.841 [0.807-0.876]
Adjusting for Child's Characteristics**				
Underweight	1.149 [1.908-1.455]	1.116 [0.808-1.542]	1.267 [0.821-1.955]	0.638 [0.542-0.751]
Normal	1.059 [0.984-1.140]	0.916 [0.819-1.024]	0.953 [0.06-1.125]	0.689 [0.654-0.727]
Overweight	1.071 [0.997-1.152]	0.992 [0.888-1.109]	0.742 [0.611-0.902]	0.681 [0.642-0.721]
Obese	1.120 [1.065-1.178]	1.022 [0.946-1.105]	0.982 [0.865-1.115]	0.748 [0.718-0.779]
Adjusting for Mother and Child's Characteristics***				
Underweight	1.149 [1.908-1.455]	1.116 [0.808-1.542]	1.267 [0.821-1.955]	0.638 [0.542-0.751]
Normal	1.059 [0.984-1.140]	0.916 [0.819-1.024]	0.953 [0.06-1.125]	0.689 [0.654-0.727]
Overweight	1.071 [0.997-1.152]	0.992 [0.888-1.109]	0.742 [0.611-0.902]	0.681 [0.642-0.721]
Obese	1.120 [1.065-1.178]	1.022 [0.946-1.105]	0.982 [0.865-1.115]	0.748 [0.718-0.779]

*Adjusted for mother's characteristics of maternal age, maternal race, mother's education, pre-pregnancy diabetes and gestational diabetes
 **Adjusted for child's characteristics of gestational age at birth, infant sex and birthweight
 ***Adjusted for mother and child's characteristic of maternal age, maternal race, mother's education, pre-pregnancy diabetes, gestational diabetes, gestational age at birth, infant sex and birthweight

Table 4. Adjusted Odds Ratios and Confidence Intervals of Eclampsia by Maternal Pre-pregnancy BMI Category and Smoking Status in Comparison to Non-smokers

	Quit before Pregnancy	Quit after First Trimester	Quit after Second Trimester	Smoked throughout Pregnancy
Adjusting for Mother's Characteristics*				
Underweight	1.154 [0.912-1.462]	1.188 [0.860-1.641]	1.623 [1.059-2.488]	0.808 [0.683-0.956]
Normal	1.092 [1.015-1.175]	1.007 [0.902-1.126]	1.184 [1.004-1.395]	0.913 [0.865-0.963]
Overweight	1.103 [1.027-1.186]	1.065 [0.954-1.190]	0.883 [0.728-1.070]	0.853 [0.804-0.905]
Obese	1.107 [1.053-1.164]	1.039 [0.962-1.122]	1.067 [0.942-1.209]	0.841 [0.807-0.876]
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Adjusting for Mother and Child's Characteristics***				
Underweight	1.149 [1.908-1.455]	1.116 [0.808-1.542]	1.267 [0.821-1.955]	0.638 [0.542-0.751]
Normal	1.059 [0.984-1.140]	0.916 [0.819-1.024]	0.953 [0.06-1.125]	0.689 [0.654-0.727]
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*Adjusted for mother's characteristics of maternal age, maternal race, mother's education, pre-pregnancy diabetes and gestational diabetes
 **Adjusted for child's characteristics of gestational age at birth, infant sex and birthweight
 ***Adjusted for mother and child's characteristic of maternal age, maternal race, mother's education, pre-pregnancy diabetes, gestational diabetes, gestational age at birth, infant sex and birthweight

DISCUSSION

This study found an increase in the odds of GH in mothers who quit before pregnancy in comparison to non-smokers in all pBMI strata. Additionally, results suggest decreased odds in GH amongst mothers smoking throughout pregnancy compared to non-smokers in all pBMI strata. In general, these findings are in accordance with similar studies conducted in the United States.^{15,16} Additionally, our results suggest that mothers who quit during any trimester experience no significant change in risk of GH, which supports but, also contradicts the findings of previous studies.^{14,15} Furthermore, this study concurrently investigated the effects of maternal smoking on eclampsia, and it was observed that smoking was not generally associated with eclampsia. Understanding the timing of smoking during pregnancy, as well as the initiation of cessation, in relation to HDP can help identify more at-risk mothers in clinical settings and optimize preventative measures.

The findings for GH in this study are like existing literature however, some disagreement is seen in the risk of GH when quitting before pregnancy or after the second trimester.^{14-16,19}

For example, England et al¹⁴ used data from select US medical centers from 1992 to 1995 and found that mothers who smoked during pregnancy has reduced risks of hypertension and preeclampsia. Like the current study, they found that mothers who smoked during pregnancy had reduced risks of GH compared to non-smokers (RR: 0.8; 95% CI: 0.6-0.9),¹⁴ however, for those mothers quitting before pregnancy, they found no significant effect on risk of GH (RR: 1.1; 95% CI, 0.9-1.3),¹⁴ but our results suggested that there were risk associations regardless of body mass status, which went along with a study conducted by Wang et al¹⁵ in which they found that women who quit before the start of pregnancy had a higher risk of GH than non-smokers (RR 1.02; 95% CI: 1.00-1.05).

Wang et al¹⁵ found that mothers who quit before the third trimester were at an increased risk (RR 1.08; 95% CI 1.02-1.16), which differs from what we observed, i.e., quitting at any point during pregnancy was not generally significant for GH regardless their body mass status. These differences may be attributable to the methods used in the analysis, stratifying BMI as well as maternal smoking status in ours as opposed to just treating them as a covariate in theirs. In addition, unlike other US studies, we only focused on the mothers aged 20-29, this might partially explain that the results from ours differed from others. As most data derived from US population, the results from this study also suggest a decrease in risk of HDP when smoking during pregnancy.^{14,15} However, it should be noted that studies conducted in Japan, Poland and Russia have observed either an increase or no change in the risk of HDP in women who smoke during pregnancy.^{12,13,19} Hayashi et al¹² reported opposing findings using data from a case cohort studying 180,855 women in Japan. They found that compared to non-smokers, smokers during pregnancy were at a higher risk of pregnancy-induced hypertension (RR: 1.20; 95% CI: 1.01-1.41).¹² Similarly, research on a Polish study sample of 912 women by Lewandoska et al¹³ suggest that in comparison to mothers who never smoked, there was an increased risk of gestational hypertension

and preeclampsia in those who smoked during their first trimester and/or quit during pregnancy (Adjusted OR: 4.75, $p < 0.001$; Adjusted OR: 11.63, $p \leq 0.0001$). Alternatively, a prospective cohort study of 39,566 women conducted in Russia reported that women who continued to smoke had no significant change in risk of preeclampsia/eclampsia compared to those who quit smoking before pregnancy (OR: 1.10 with 95% CI: 0.91-1.32).¹⁹ This observation suggests that the relationship of smoking during pregnancy and HDP could be dependent on geographic location and population characteristics.² The non-US studies also used relatively smaller sample sizes, which may also account for the different relationships observed compared to larger US-based studies like ours (n: 1,376,271) and Wang et al¹⁵ (n: 3,319,223).

A study out of Washington State saw an inverse association between smoking at any time during pregnancy and eclampsia risk which slightly differs from our findings as only normal and obese mothers who smoked throughout pregnancy had significantly lower ORs.¹⁶ In contrast to Coghill et al¹⁶ the current study stratified by pBMI, which may account for this difference.

Indeed, we need to be aware of any limitation of the study when interpreting the results. First, since smoking status on birth records is self-reported so there may be some under-reporting and possible misclassification. Furthermore, there may be some variation in the gestational ages used to define trimesters by mothers reporting smoking data. Second, the variable of GH also included mothers who have PE meaning pregnancy-induced hypertension and PE cannot be evaluated separately. The relation of smoking during pregnancy to pregnancy-induced hypertension and PE may differ which would be important for gauging clinical outcomes since women with PE are more likely to progress to eclampsia which can be lethal.¹¹ Thirdly, it cannot be ensured that the diagnostic criteria for HDPs were the same across all diagnoses performed as data was created using information from birth certificate data collected in different settings and locations across the United States. Lastly, there is the possibility of unaccounted for confounding bias by unmeasured factors. Specifically, those indicative of nutrition, access to healthcare, experiences of prejudice and/or discrimination, or mental health, particularly stress and anxiety. Nevertheless, a clear merit of the study is that a large population-based dataset represents well of US mothers aged 20-29 population regarding the research question we have explored.

CONCLUSION

In summary, an increase in the odds of GH were observed amongst normal, overweight, and obese mothers quitting before pregnancy meanwhile a decreased odds were observed amongst mothers smoking throughout pregnancy in all pBMI classes. Additionally, the study observed that smoking was generally not associated with eclampsia.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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