HHS Public Access

Author manuscript

World J Pediatr. Author manuscript; available in PMC 2023 October 13.

Published in final edited form as:

World J Pediatr. 2022 August ; 18(8): 568–573. doi:10.1007/s12519-022-00571-z.

Race as a moderator of the association between ethnicity, preeclampsia and neonatal respiratory distress syndrome

Boubakari Ibrahimou[1], **Ning Sun**[1], **Shelbie Burchfield**[1], **Priyanka Shrestha**[1], **Fernanda Veitzman**[1], **Zoran Bursac**[1], **Hamisu Salihu**[2], **Getachew Dagne**[3], **Janvier Gasana**[4], **Tomas R. Guilarte**[5]

[1]Department of Biostatistics, Florida International University, Robert Stempel College of Public Health and Social Work, 11200 S.W. 8th Street, AHC5, Miami, FL 33199, USA

[2]Center of Excellence in Health Equity, Training and Research, Baylor College of Medicine, One Baylor Plaza MS: 411, Houston, TX 77030, USA

[3]College of Public Health, University of South Florida, 13201 Bruce B. Downs Blvd, MDC 56, Tampa, FL 33612, USA

[4]Faculty of Public Health, Department of Environmental and Occupational Health, Kuwait University, Block 7 Street 32013119, PO Box 24923, Safat, Hawally, Kuwait

[5]Department of Environmental Health Sciences, Florida International University, Robert Stempel College of Public Health and Social Work, 11200 S.W. 8th Street, AHC5, Miami, FL 33199, USA

Neonatal respiratory distress syndrome (RDS), also known as hyaline membrane disease, is a leading cause of neonatal mortality in the US, which affects 1% of all newborns and 10% of preterm babies [1, 2]. It is also one of the most common causes of admission to neonatal intensive care unit [3]. Preeclampsia (PE) is a common pregnancy complication that affects an estimated 5% of pregnancies across the world [4]. It is a significant cause of low birth weight and preterm delivery, which are risk factors for RDS [5]. However, in the literature, the relationship between PE and RDS remains controversial [6–9].

The occurrences of both PE and RDS vary among difference races. Literature shows that Black or Asian infants have lower incidence rates of RDS compared to White infants [10–13]. Disproportional occurrence of PE among race groups was also noticed, as non-Hispanic Black infants are more severely affected compared to White infants [14, 15]. Therefore, building on the existing literature, we hypothesized that the effect of PE on RDS would be differentiated by race. Meanwhile, we are also interested in the effect of being Hispanic on

✉Boubakari Ibrahimou, bibrahim@fiu.edu.

Author contributions IB contributed to conceptualization, design, data acquisition/analysis/interpretation, funding acquisition, and drafting. SN and BS contributed to analysis, writing, review and editing. SP contributed to design and writing of the original draft. VF contributed to data curation, interpretation of data, and critically revising. BZ, SH, DG, GJ, and GTR contributed to concept and design, and critically revising. All the authors approved the final version of the manuscript.

Conflict of interest No financial or non-financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article. The authors have no conflict of interest to declare.

Ethical approval The Institutional Review Board (IRB) of Florida International University as well as the Florida Department of Health IRB reviewed this study and deemed it exempt. Informed consent to participate in the study have been obtained from participants (or their parent or legal guardian in the case of children under 16).

RDS incidence among subgroups of Hispanic by race. Hispanics in the US are generally studied as a single ethnic group, but it is a culturally heterogeneous group, by country of origin or generation of immigration. This study aims to explore the modification effect of race on PE and ethnicity leading to RDS. We included full-term infants in the analysis besides preterm newborns and found some differences between the two subgroups.

De-identified birth records data from 2011 to 2020 provided by the Florida Bureau of Vital Statistics were used in this study. The Institutional Review Board (IRB) of Florida International University as well as the Florida Department of Health IRB reviewed this study and deemed it exempt. Informed consent to participate in the study have been obtained from participants (or their parent or legal guardian in the case of children under 16). Both PE and RDS were recorded in the dataset as Yes/No. Due to the small size of American Indian or Alaskan Native (AIAN), and other Pacific islander (NPI) in the data, race was categorized as White, Black, Asian or Pacific islander, and others (including other races, AIAN and multiple races). Ethnicity was defined as non-Hispanic/Hispanic. Covariates include demographic variables (maternal age, education level, ethnicity), behavior variables [tobacco and alcohol usage during pregnancy, prenatal care, and WIC (women, infants and children) program status], pregnancy-related variables (gestational weeks, birth weight, birth route, plurality, infant sex), and mother's medical information (body mass index, history of diabetes, gestational diabetes, history of preterm birth, and premature rupture of membrane).

Births from mothers with eclampsia were excluded from the sample. A total of 2,219,144 infants, including 12,577 (0.57%) cases born with RDS (Table 1) were included in the study. Infants born to preeclamptic women had 2.63 times the odds of developing RDS compared to those born to non-preeclamptic women [odds ratio (OR) = 2.63, 95% confidence interval (CI) 2.50–2.76]. Compared to their White counterparts, Black race (OR = 1.64, 95% CI 1.58–1.70) was associated with higher odds of having RDS and Asian American race (OR = 0.89, 95% CI 0.79–0.99) was associated with lower odds of RDS. Being Hispanic (OR = 0.93, 95% CI 0.88–0.97) was also associated with lower odds of having RDS (Table 1).

Table 2 shows the adjusted odds ratios (aOR) and 95% CI of having RDS after controlling for potential confounders. Gestational subgroup analyses were conducted for preterm (< 37 gestational weeks) and full-term infants (≥ 37 gestational weeks) separately. Three important interactions were identified in the models. The two subgroups showed different patterns on the interactions.

Interaction between race and PE was detected in full-sample (PE:Black, aOR = 0.80, 95% CI 0.71–0.89) and the full-term group (PE:Black, aOR = 0.71, 95% CI 0.58–0.88). In other words, the adverse effect of PE was significantly lessened by Black race among full-term infants but not preterm infants. While controlling for other covariates for full-term infants, the risk of RDS increased by 75% for infants from non-Hispanic White mothers having maternal PE compared to non-Hispanic Whites without PE, and the increased risk was damped to 30% for infants from mothers with PE among non-Hispanic Black race, compared with the same reference group (Table 3). For preterm infants, the corresponding two ratios of having RDS for the same group comparisons were 1.15 and 0.93, respectively (Table 3). As RDS among full-term and preterm infants are majorly caused by different

factors [16], the differences seen in the current study are expected. The mechanisms underlying such disparities are currently unclear. Lower serum level of surfactant protein A (SP-A) is associated with RDS incidence and severity. Some previous studies revealed that SP-A and/or SP-B genetic variants may be associated with race differences of RDS incidence among Black and White races, and specific genotypes appear to be a protective factor for Blacks but not for Whites [17, 18]. Additionally, a lower serum level of SP-A was associated with early-onset PE [19]. These concurrent associations suggest a possible explanation for the racial difference of the association between race and PE. However, further biological studies are needed to clarify the patterns.

Black and Asian races modified the effect of maternal Hispanic ethnicity on neonatal RDS for the full-sample as well as the preterm and full-term subgroups. The modification was smaller in the preterm group (Black:Hispanic, aOR = 1.90, 95% CI 1.70–2.13; Asian:Hispanic, aOR = 2.16, 95% CI 1.03–4.54) compared to the full-term group (Black:Hispanic, aOR = 2.40, 95% CI 2.11–2.73; Asian:Hispanic, aOR = 5.35, 95% CI 3.00–9.55). Even though being Hispanic White was associated with lower risk of neonatal RDS compared to non-Hispanic White group, self-identification as Hispanic was associated with higher risk of RDS for Black race or Asian race. With other covariates controlled for, preterm infants born to Hispanic Black or Hispanic Asian mothers were 1.47 and 1.43 times as likely to have RDS compared to those of non-Hispanic White mothers, respectively (Table 3). For full-term infants, the respective odds were 1.79 and 3.04 for the same comparison groups. A possible reason for the racial differences observed is that Hispanic Whites may be more acculturated compared to the other groups. That means some unmeasured social determinants may be different here, such as socioeconomic status, language barriers to medical treatment/care, or cultural beliefs or practices [20]. Because of this, it is important to investigate racial differences among Hispanic subgroups, and this is the first study to do so for the risk of RDS. Besides the modification effect of race on PE and ethnicity, the interaction between PE and premature rupture of membrane before labor (PRoM) was noticed. PRoM lessens the risk of RDS for the preterm group (aOR = 0.63, 95% CI 0.50–0.79) but increases the risk for the full-term group (aOR = 1.65, 95% CI 1.02–2.65).

Our findings identified preterm newborns from Hispanic Black/Hispanic Asian women with PE, full-term infants from preeclamptic non-Hispanic White women or from Hispanic Black/Hispanic Asian women regardless their PE condition as potentially vulnerable subgroups of acquiring RDS in their term group. Health care institutions should take the disparity observed here into consideration when providing prenatal care or preventative treatments. Special interventions for the identified vulnerable subgroups should be developed and evaluated. For example, provide culturally tailored materials about the risk and prevention strategies of PE; enhance clinical-community partnerships that help screen and support social determinants of health among Hispanic Black/Asian mothers, such as social isolation, parental education, and financial stress; increase their access to high-quality healthcare, and prepare for appropriate follow-up of these high-risk newborns.

This study has some limitations. Gestational hypertension was not separated from PE, and the severity of RDS and the onset stage of PE were not included in the analysis because

of the restriction of data. Additional analysis with these features considered might be promising.

Funding

This work is supported by the National Heart Lung and Blood Institute (No. K01 HL146944), the National Institute on Minority Health and Health Disparities of the National Institutes of Health (No. U54MD012393), FIU-RCMI and the FL-DOH.

Data availability

The datasets generated during and/or analyzed during the current study are not publicly available due to the Florida Department of Health Data Use agreement restriction but are available from the Florida Department of Health, Bureau of Vital Statistics on reasonable request.

References

1. Reuter S, Moser C, Baack M. Respiratory distress in the newborn. Pediatr Rev. 2014;35:417–28; quiz 429. [PubMed: 25274969]
2. Rubarth LB, Quinn J. Respiratory development and respiratory distress syndrome. Neonatal Netw. 2015;34:231–8. [PubMed: 26802638]
3. Horowitz K, Feldman D, Stuart B, Borgida A, Ming Victor Fang Y, Herson V. Full-term neonatal intenstive care unit admission in an urban community hospital: the role of respiratory morbidity. J Matern Fetal Neonatal Med. 2011;24:1407–10. [PubMed: 21299397]
4. Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. Nat Rev Nephrol. 2019;15:275–89. [PubMed: 30792480]
5. Madazli R, Yuksel MA, Imamoglu M, Tuten A, Oncul M, Aydin B, et al. Comparison of clinical and perinatal outcomes in early- and late-onset preeclampsia. Arch Gynecol Obstet. 2014;290:53–7. [PubMed: 24549271]
6. Langenveld J, Ravelli AC, van Kaam AH, van der Ham DP, van Pampus MG, Porath M, et al. Neonatal outcome of pregnancies complicated by hypertensive disorders between 34 and 37 weeks of gestation: a 7 year retrospective analysis of a national registry. Am J Obstet Gynecol. 2011;205:e1–7.
7. Tian T, Wang L, Ye R, Liu J, Ren A. Maternal hypertension, preeclampsia, and risk of neonatal respiratory disorders in a large-prospective cohort study. Pregnancy Hypertens. 2020;19:131–7. [PubMed: 31982835]
8. Wen Y, Yang HI, Chou HC, Chen CY, Hsieh WS, Tsou KI, et al. Association of maternal preeclampsia with neonatal respiratory distress syndrome in very-low-birth-weight infants. Sci Rep. 2019;9:13212. [PubMed: 31519996]
9. Masoura S, Kalogiannidis I, Margioula-Siarkou C, Diamanti E, Papouli M, Drossou-Agakidou V, et al. Neonatal outcomes of late preterm deliveries with pre-eclampsia. Minerva Ginecol. 2012;64:109–15. [PubMed: 22481621]
10. Nguyen BT, Cheng YW, Snowden JM, Esakoff TF, Frias AE, Caughey AB. The effect of race/ethnicity on adverse perinatal outcomes among patients with gestational diabetes mellitus. Am J Obstet Gynecol. 2012;207:e1–6.
11. Thomas PE. Do racial disparities persist in infant mortality from respiratory distress syndrome? J Obstet Gynecol Neonatal Nurs. 2011;40:47–51.
12. Cox AG, Narula S, Malhotra A, Fernando S, Wallace E, Davies-Tuck M. The influence of maternal ethnicity on neonatal respiratory outcome. Arch Dis Child Fetal Neonatal Ed. 2020;105:50–5. [PubMed: 31123055]

13. Anadkat JS, Kuzniewicz MW, Chaudhari BP, Cole FS, Hamvas A. Increased risk for respiratory distress among white, male, late preterm and term infants. J Perinatol. 2012;32:780–5. [PubMed: 22222548]
14. Tanaka M, Jaamaa G, Kaiser M, Hills E, Soim A, Zhu M, et al. Racial disparity in hypertensive disorders of pregnancy in New York State: a 10-year longitudinal population-based study. Am J Public Health. 2007;97:163–70. [PubMed: 17138931]
15. Ghosh G, Grewal J, Männistö T, Mendola P, Chen Z, Xie Y, et al. Racial/ethnic differences in pregnancy-related hypertensive disease in nulliparous women. Ethn Dis. 2014;24:283–9. [PubMed: 25065068]
16. Stylianou-Riga P, Boutsikou T, Kouis P, Kinni P, Krokou M, Ioannou A, et al. Maternal and neonatal risk factors for neonatal respiratory distress syndrome in term neonates in Cyprus: a prospective case–control study. Ital J Pediatr. 2021;47:129. [PubMed: 34082803]
17. Floros J, Fan R, Diangelo S, Guo X, Wert J, Luo J. Surfactant protein (SP) B associations and interactions with SP-A in white and black subjects with respiratory distress syndrome. Pediatr Int. 2001;43:567–76. [PubMed: 11737731]
18. Kale K, Vishwekar P, Balsarkar G, Jassawalla MJ, Sawant G, Madan T. Differential levels of surfactant protein A, surfactant protein D, and progesterone to estradiol ratio in maternal serum before and after the onset of severe early-onset preeclampsia. Am J Reprod Immunol. 2020;83:e13208. [PubMed: 31702086]
19. Ndwiga C, Odwe G, Pooja S, Ogutu O, Osoti A, Warren CE. Clinical presentation and outcomes of pre-eclampsia and eclampsia at a national hospital, Kenya: a retrospective cohort study. PLoS One. 2020;15:e0233323. [PubMed: 32502144]
20. Gonzalez Burchard E, Borrell LN, Choudhry S, Naqvi M, Tsai HJ, Rodriguez-Santana JR, et al. Latino populations: a unique opportunity for the study of race, genetics, and social environment in epidemiological research. Am J Public Health. 2005;95:2161–8. [PubMed: 16257940]

Table 1

Baseline descriptive statistics for Florida birth records from 2011 to 2020

Variables	Respiratory distress syndrome		Odds ratio[a] (95% CI)
	No (*n* = 2,206,567), *n* (%)	Yes (*n* = 12,577), *n* (%)	
Preeclampsia			
No	2,071,643 (93.89)	10,738 (85.38)	Reference
Yes	134,924 (6.11)	1839 (14.62)	2.63 (2.50–2.76)
Mother's age (y)			
18–35	1,788,828 (81.07)	9779 (77.75)	Reference
< 18	31,285 (1.42)	185 (1.47)	1.08 (0.93–1.25)
> 35	386,454 (17.51)	2613 (20.78)	1.24 (1.18–1.29)
Mother's educational level			
≥ High school graduate	1,932,284 (87.57)	10,525 (83.68)	Reference
< High school graduate	274,283 (12.43)	2052 (16.32)	1.37 (1.31–1.44)
Mother's race			
White	1,576,416 (71.44)	7897 (62.79)	Reference
Black	491,463 (22.27)	4034 (32.07)	1.64 (1.58–1.70)
Asian and Pacific islander	69,106 (3.13)	307 (2.44)	0.89 (0.79–0.99)
Other	69,582 (3.15)	339 (2.70)	0.97 (0.87–1.08)
Mother's ethnicity			
Non-hispanic	1,461,282 (66.22)	8437 (67.08)	Reference
Hispanic	745,285 (33.78)	4140 (32.92)	0.93 (0.88–0.97)
WIC nutrition			
No	1,157,293 (52.45)	6012 (47.8)	Reference
Yes	1,049,274 (47.55)	6565 (52.20)	1.20 (1.16–1.25)
Tobacco use by mother			
No	2,098,393 (95.10)	11,821 (93.99)	Reference
Yes	108,174 (4.90)	756 (6.01)	1.24 (1.15–1.33)
Prenatal care received			
Yes	2,174,307 (98.54)	12,094 (96.16)	Reference
No	32,260 (1.46)	483 (3.84)	2.69 (2.45–2.95)

Variables	Respiratory distress syndrome		Odds ratio[a] (95% CI)
	No (*n* = 2,206,567), *n* (%)	Yes (*n* = 12,577), *n* (%)	
Mother's history of diabetes			
No	2,187,918 (99.15)	12,299 (97.79)	Reference
Yes	18,649 (0.85)	278 (2.21)	2.65 (2.35–2.98)
Gestational diabetes			
No	2,089,199 (94.68)	11,467 (91.17)	Reference
Yes	117,368 (5.32)	1110 (8.83)	1.72 (1.62–1.83)
Alcohol use			
No	2,195,348 (99.49)	12,467 (99.13)	Reference
Yes	11,219 (0.51)	110 (0.87)	1.74 (1.43–2.09)
Mother's history of preterm birth			
No	2,172,389 (98.45)	11,813 (93.93)	Reference
Yes	34,178 (1.55)	764 (6.07)	4.11 (3.82–4.42)
BMI			
< 30	1,695,737 (76.85)	8999 (71.55)	Reference
≥ 30	510,830 (23.15)	3578 (28.45)	1.32 (1.27–1.37)
Premature rupture of membrane before labor			
No	2,133,645 (96.7)	11,204 (89.08)	Reference
Yes	72,922 (3.30)	1373 (10.92)	3.59 (3.39–3.79)
Birth route			
No cesarean	1,389,553 (62.97)	4821 (38.33)	Reference
Cesarean	817,014 (37.03)	7756 (61.67)	2.74 (2.64–2.84)
Plurality			
Singleton	2,137,044 (96.85)	10,832 (86.13)	Reference
Twin	67,378 (3.05)	1617 (12.86)	4.74 (4.49–4.99)
Multiples (3–5)	2145 (0.10)	128 (1.02)	11.79 (9.80–14.04)
Infant sex			
Female	1,077,618 (48.84)	5305 (42.18)	Reference
Male	1,128,949 (51.16)	7272 (57.82)	1.31 (1.26–1.36)
Infant's weight (g)			
≥ 2500	2,025,173 (91.78)	6335 (50.37)	Reference

Variables	Respiratory distress syndrome		Odds ratio[a] (95% CI)
	No (*n* = 2,206,567), *n* (%)	Yes (*n* = 12,577), *n* (%)	
< 2500	181,394 (8.22)	6242 (49.63)	11.00 (10.62–11.40)
Infant gestation week (wk)			
≥ 37	1,991,265 (90.24)	5334 (42.41)	Reference
34–37	155,143 (7.03)	2729 (21.70)	6.57 (6.27–6.88)
< 34	60,159 (2.73)	4514 (35.89)	28.01 (26.90–29.19)

CI confidence interval, *BMI* body mass index, *WIC* women, infants and children.

[a]Odds ratio for univariate logistic analysis

Table 2

Odds ratio of respiratory distress syndrome occurrence from multivariable models

Variables	Model A[a] (full sample)	Model B[a] (preterm)	Model C[a] (full-term)
Interactions			
Race:ethnicity			
Black:Hispanic	2.12 (1.94–2.31)*	1.90 (1.70–2.13)*	2.40 (2.11–2.73)*
Asian:Hispanic	3.44 (2.16–5.46)*	2.16 (1.03–4.54)*	5.35 (3.00–9.55)*
Others:Hispanic	1.31 (1.02–1.68)*	1.30 (0.93–1.82)	1.32 (0.90–1.92)
Preeclampsia:race			
Preeclampsia:Black	0.80 (0.71–0.89)*	0.91 (0.80–1.03)	0.71 (0.58–0.88)*
Preeclampsia:Asian	0.85 (0.58–1.23)	1.07 (0.70–1.64)	0.48 (0.20–1.19)
Preeclampsia:others	0.99 (0.72–1.35)	1.11 (0.77–1.61)	0.84 (0.45–1.56)
Preeclampsia:PRoM			
Preeclampsia:mother having PRoM	0.73 (0.59–0.89)*	0.63 (0.50–0.79)*	1.65 (1.02–2.65)*
Preeclampsia:gestational week			
Preeclampsia:< 34 wk	0.68 (0.60–0.77)*	NA	NA
Preeclampsia:34–37 wk	0.67 (0.58–0.76)*	NA	NA
Main effects			
Preeclampsia			
No	Reference	Reference	Reference
Yes	1.78 (1.62–1.97)*	1.15 (1.06–1.24)*	1.75 (1.56–1.96)*
Mother’s race			
White	Reference	Reference	Reference
Black	0.94 (0.89–0.99)*	0.89 (0.83–0.95)*	1.05 (0.97–1.14)
Asian and Pacific islander	0.80 (0.70–0.91)*	0.76 (0.63–0.91)*	0.80 (0.67–0.96)*
Other	0.85 (0.74–0.98)*	0.82 (0.68–0.99)*	0.88 (0.72–1.06)
Mother’s ethnicity			
Non-hispanic	Reference	Reference	Reference
Hispanic	0.79 (0.75–0.83)*	0.87 (0.81–0.92)*	0.71 (0.66–0.76)*

Variables	Model A[a] (full sample)	Model B[a] (preterm)	Model C[a] (full-term)
Tobacco use by mother			
No	Reference	Reference	Reference
Yes	0.92 (0.85–0.99) *	0.81 (0.73–0.90) *	1.02 (0.91–1.15)
PRoM			
No	Reference	Reference	Reference
Yes	1.38 (1.30–1.47) *	1.59 (1.49–1.71) *	1.13 (0.94–1.35)
Infant gestation week (wk)			
≥ 37	Reference	Reference	Reference
34–37	4.37 (4.11–4.64) *	NA	NA
< 34	12.93 (12.02–13.91) *	NA	NA

PRoM premature rupture of membrane before labor, *BMI* body mass index, *WIC* women, infants and children, *NA* not available.

[a]Models were adjusted by maternal age, education level, BMI, prenatal care status, alcohol use during pregnancy, WIC program status, birth route, plurality, infant's weight, sex, maternal history of diabetes, history of preterm birth, gestational diabetes.

*$P < 0.05$

Table 3

Respiratory distress syndrome occurrence risk for race/eth- nicity/preeclampsia groups

Variables	Full sample	Preterm	Full-term
White			
Non-Hispanic, non-preelamp- tic	Reference	Reference	Reference
Non-Hispanic, preelamptic	1.78	1.15	1.75
Hispanic, non-preelamptic	0.79	0.87	0.71
Hispanic, preelamptic	1.41	1.00	1.24
Black			
Non-Hispanic, non-preelamp- tic	0.94	0.89	1.05
Non-Hispanic, preelamptic	1.34	0.93	1.30
Hispanic, non-preelamptic	1.57	1.47	1.79
Hispanic, preelamptic	2.24	1.54	2.22
Asian			
Non-Hispanic, non-preelamp- tic	0.80	0.76	0.80
Non-Hispanic, preelamptic	1.21	0.94	0.67
Hispanic, non-preelamptic	2.17	1.43	3.04
Hispanic, preelamptic	3.29	1.76	2.55
Others			
Non-Hispanic, non-preelamp- tic	0.85	0.82	0.88
Non-Hispanic, preelamptic	1.50	1.05	0.85
Hispanic, non-preelamptic	0.88	0.93	0.82
Hispanic, preelamptic	1.55	1.18	1.21