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Letter to the Editor

Increased risk of eclampsia and preeclampsia during delivery hospitalizations in women with beta-thalassemia; An analysis of the National Inpatient Sample database

Dear Editor,

The rate of successful pregnancies among women with beta-thalassemia (b-thal) has been on the rise because of the widespread use of iron chelators as most women now live well past their childbearing age [1]. Although patients with compromised cardiac function from iron overload have a high likelihood of postpartum complications and are often advised against pregnancy, there is limited data for obstetrical risks in asymptomatic pregnant women with b-thal. To evaluate this, we conducted a retrospective study using the National Inpatient Sample (NIS) database to identify if significant differences were present in the rates of eclampsia and preeclampsia.

We analyzed NIS data from 2002 to 2019 using International Classification of Diseases, 9th and 10th Revision, Clinical Modification/ Procedure Coding System (ICD-9–CM/ PCS) (Supplemental Index Table 1). We first identified delivery hospitalizations in patients > 18 years of age using the ICD-10 CM codes. Thereafter we identified patients with b-thal. We removed any cases with missing data for age, gender, or race. Statistical descriptions were presented as frequencies and percentages for categorical variables and as medians and interquartile ranges for continuous variables. In the case of categorical variables, Chi square test and Fisher exact test were used, whereas in the case of continuous variables, Mann-Whitney U was used. We calculated unadjusted odds ratios (uORs) using the Cochrane-Mantel-Haenszel test [2]. An analysis of b-thal and in-hospital outcomes was conducted using a hierarchical multivariate logistic regression model adjusted for age, race, ethnicity, hospital region, and comorbid conditions listed in Table 1.

A total of 59,540,417 weighted hospitalizations for deliveries were identified in the United States from 2002 to 2019. Of the included patients, 6530 (0.01 %) had a diagnosis of b-thal. Patients with b-thal had a higher median (interquartile range) age of 30 (26–34) years compared with 28 (24–32) years for patients without b-thal ($p < 0.01$). Women with b-thal were more likely to be Asian race (20.9 % versus 5.5 %) and less likely to be White (36.1 % versus 52.7 %). In regard to baseline comorbidities, gestational diabetes (8.7 % versus 3.1 %), obesity (5.4 % versus 2.3 %), and liver disease (2.2 % versus 0.1 %) were more frequent in the b-thal group when compared with patients without b-thal (Table 1). After adjustment for age, race and ethnicity, comorbidities, insurance, and income, b-thal patients had higher odds of preeclampsia (adjusted (a) OR: 1.16 [95 % CI, 1.04–1.29]; $p < 0.01$) and eclampsia (aOR, 2.20 [95 % CI, 1.48–3.26]; $p < 0.01$). Deliveries for women with b-thal also had a higher cost of hospitalization ($4901 versus $3616; $p < 0.01$) (Table 1).

We hypothesize that the increased rate of preeclampsia and eclampsia are likely driven by the anemia caused by b-thal. The reduced oxygen capacity in b-thal causes the release of hypoxia induced cytokines like soluble fms-like tyrosine kinase-1 (sFlt-1) that induce remodeling of spiral arteries and placental trophoblasts [3]. These cascading events lead to endothelial dysfunction which forms the pathologic basis of preeclampsia and eclampsia [4]. Since pregnancy induced hemodilution causes a further decrease in Hb, patients with b-thal should be transfused at the preconception goal to decrease risk of these complications [1].

Though we attempted to account for potential confounders by using a robust logistic regression model, our study still has limitations inherent to the NIS database. Firstly, the data is retrospective and can be used to establish correlation. Secondly, each case represents a separate hospitalization and not individual patient data so there may be multiple hospitalizations captured for the same patient with recurrent admissions, i.e., recurrent pregnancies. However, despite these limitations, our study emphasizes the need for prenatal evaluation for risk stratification to decrease the risk of preeclampsia and eclampsia in women with b-thal.

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Table 1
Summary of the univariate, multivariate and cost analysis.

Variable no. (%)	Univariate analysis		
	Beta thalassemia (N = 59,540,417)	**without beta-thalassemia (N = 6530)**	**P value**
Age (Interquartile range) years	30 (26–34)	28 (24–32)	< 0.01
Racial, and socioeconomic characteristics:			
Race			< 0.01
White	2359 (36.1)	31,382,863 (52.7)	
Black	1613 (24.7)	8,374,865 (14.1)	
Hispanic	600 (9.2)	13,215,163 (22.2)	
Asian or Pacific Islanders	1363 (20.9)	3,273,394 (5.5)	
Other	595 (9.1)	3,294,546 (5.5)	
Insurance Payee			< 0.01
Medicare	11,740 (75.0)	341,282 (52.9)	
Medicaid	582 (3.7)	82,447 (12.8)	
Private Insurance	2937 (18.8)	182,852 (28.3)	
Other	388 (2.5)	39,107 (6.0)	
Median household income			< 0.01
1st–25th Percentile	1477 (22.9)	15,718,651 (26.8)	
26th–50th Percentile	1492 (23.1)	14,118,532 (24.1)	
51st–75th Percentile	1528 (23.6)	14,294,585 (24.4)	
76th–100th Percentile	1964 (30.4)	14,420,436 (24.6)	
Comorbid conditions:			
Gestational Diabetes	565 (8.7)	1,830,970 (3.1)	< 0.01
Drug Abuse	101 (1.5)	532,483 (0.9)	< 0.01
Chronic Kidney Disease	9 (< 0.1)	32,976 (0.1)	–
Hypertension	25 (0.4)	380,659 (0.6)	< 0.01
Hypothyroidism	413 (6.3)	1,474,353 (14.7)	< 0.01
Liver Disease	60 (0.9)	123,337 (0.2)	< 0.01
Obesity	350 (5.4 %)	1,358,190 (2.3)	< 0.01
Rheumatoid Disorders	30 (0.5)	160,403 (0.3)	< 0.01
Smoking	110 (1.7)	1,149,699 (1.9)	0.15
Caesarian Section	2336 (35.8)	18,789,263 (31.6)	< 0.01
Multiple gestation	200 (3.1)	1,132,978 (1.9)	< 0.01
Preterm Labor	345 (5.3)	4,364,233 (7.3)	< 0.01
Still birth	45 (0.7)	408,242 (0.7)	0.97
Hospital Location:			< 0.01
Northeast	1519 (23.3)	11,135,907 (18.7)	
Midwest	1143 (17.5)	9,787,586 (16.4)	
South	2296 (35.2)	23,700,906 (39.8)	
West	1572 (24.1)	14,916,433 (25.1)	

Multivariate analysis

Variable	Beta thalassemia[a]	Without beta thalassemia[a]	Unadjusted Odd's ratio	P value	Adjusted Odd's ratio	P value
Eclampsia	383	144	2.66 (1.76–3.94)	< 0.01	2.20 (1.48–3.26)	< 0.01
Preeclampsia	5819	4472	1.32 (1.19–1.46)	< 0.01	1.16 (1.04–1.29)	< 0.01

Cost analysis

	Beta thalassemia	Without beta thalassemia	P value
Median Total Cost of Stay ($)	16,940	11,343	< 0.01

[a] Events per 100,000 delivery hospitalizations.

Ethics approval statement

The data used for this study is publicly available and an Institutional Board Review approval was not needed.

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Conflict of Interest Disclosure

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.eurox.2022.100175.

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Mohammad Ammad Ud Din[a,b,*], Medhat Chowdhury[c], Moazzam Shahzad[a,b], Hania Liaqat[d], Michael Jaglal[a,b]
[a] *Department of Hematology & Medical Oncology, University of South Florida, Tampa, FL, the United States of America*
[b] *Department of Hematology & Medical Oncology, H Lee Moffitt Cancer Center and Research Institute, Tampa, FL, the United States of America*

[c] *Department of Cardiology, Ascension Providence Hospital, Southfield, MI, the United States of America*
[d] *Department of Internal Medicine, Rochester General Hospital, the United States of America*

[*] Correspondence to: Department of Hematology & Medical Oncology, H. Lee Moffitt Cancer and Research Institute, 12902 USF Magnolia Drive, Tampa, FL 33612, the United States of America.
E-mail address: mohammad.ammad-ud-din@moffitt.org (M. Ammad Ud Din).