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Pregnancy Complications in Women with Rare Tumor Suppressor Syndromes Affecting Central and Peripheral Nervous System

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Objective: Neurofibromatosis type 2 (NF2), tuberous sclerosis (TS), and von Hippel-Lindau disease (VHL) are tumor suppressor syndromes characterized by multiple benign tumors of the peripheral and central nervous system.¹ These tumors may lead to enhanced obstetric risk in female patients, but it is currently unknown whether women with NF2, TSC, or VHL experience increased rates of adverse pregnancy outcomes. Current data consists primarily of case series, even the largest of which may lack power due to small sample sizes.²⁻⁴

Use of large administrative databases can facilitate studies of pregnancy in rare disorders, as shown by our prior work with neurofibromatosis 1, another neurogenetic tumor suppressor syndrome. Using a population-based database, we found that pregnant women with NF1 experienced increased maternal morbidity, including higher rates of hypertensive and cerebrovascular complications, than the general population.⁵ In the current study, we apply a similar methodology to determine the association between NF2, TS, and VHL and adverse pregnancy outcomes.

Study Design: We performed a retrospective cohort study using hospital discharge data from the US Nationwide Inpatient Sample, 1998-2008. ICD-9-CM codes were used to identify pregnancy-related hospitalizations (codes 630-679) for women with NF2 (237.72), TS (759.5), or VHL (759.6). Patients were compared to a control group of all pregnancy-related hospitalizations not associated with NF1, NF2, TS, or VHL in the same time period. Admissions for women age <15 or >50 years were excluded in both groups. ICD-9 codes were used to identify pre-eclampsia, ischemic and hemorrhagic cerebrovascular disease, pre-term labor, and caesarean delivery during hospitalization, as previously described.⁵ Multivariable logistic regression was used to investigate risk of adverse outcomes in each patient population, adjusting for age, pre-existing comorbidities, race, socioeconomic status, and hospital and insurance characteristics. Statistical analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, NC). This study was approved by the Partners Institutional Review Board.

Results: Among 18,716,102 million pregnancy-associated admissions between 1988 and 2008, we identified 48 with maternal NF2, 112 with TS, and 135 with VHL. Mean maternal age was 25.5 years for TS, 26.6 years for NF2, 28.4 years for VHL, and 27.1 years for the control group. The majority of admissions for patients with tumor suppressor syndromes were at large urban teaching hospitals. Patients with TS, but not NF2 or VHL, had higher rates of pre-existing hypertension than controls (12.5% vs. 4.0%). Figure 1 presents the absolute rates, adjusted odds ratios (AOR) and 95% confidence intervals for adverse pregnancy outcomes. Patients with NF2 had significantly increased risk of pre-eclampsia (AOR, 3.5). Patients with TS had significantly increased risk of pre-eclampsia (AOR, 2.8) and preterm labor (AOR, 2.1). Patients with VHL had significantly increased risk of cerebrovascular disease (AOR, 12.5) and caesarean delivery (AOR, 1.8). No patients with NF2, TS, or VHL died during their pregnancy-related hospitalizations.

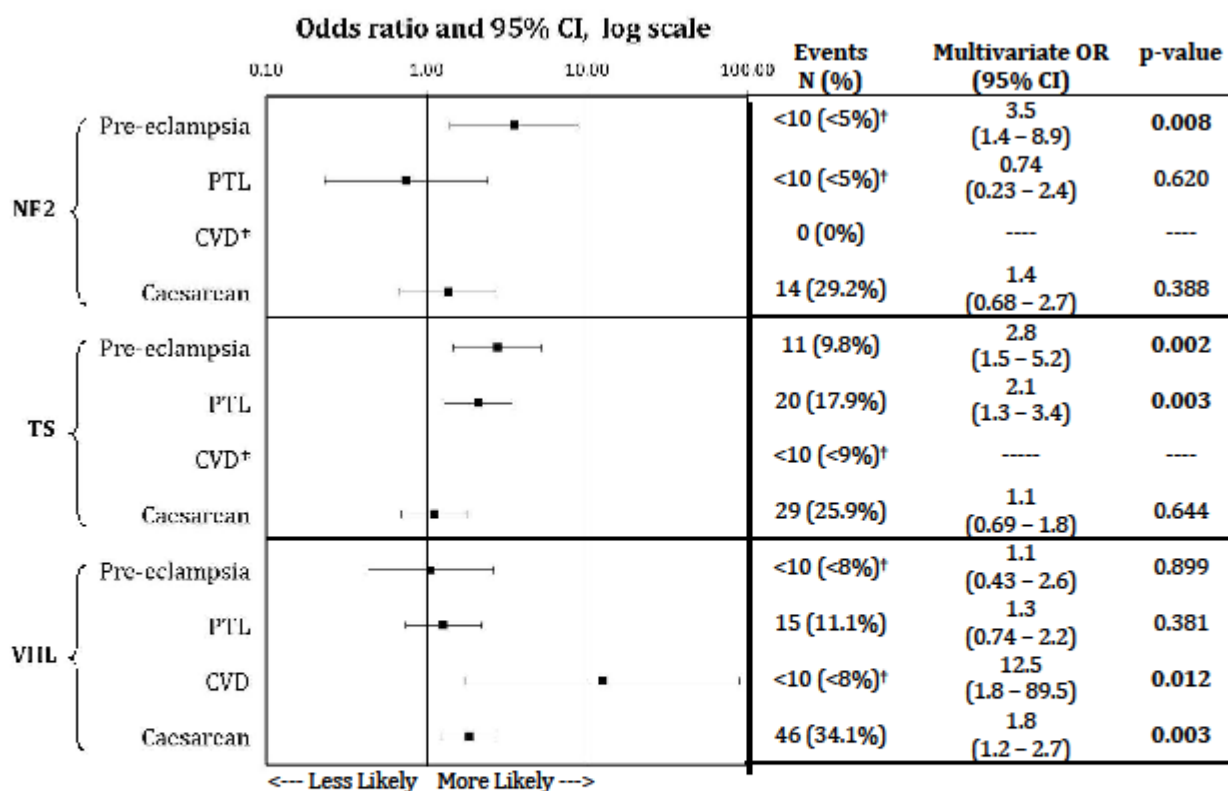
Conclusion: Women with NF2, TS, and VHL may be at risk for certain adverse pregnancy outcomes. Future research is needed to validate these findings, explore potential biological mechanisms for increased risk, and determine the impact of maternal morbidity on neonatal outcomes.

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Figure 1

Title: Multivariable odds of adverse outcomes by diagnostic category



Legend: Percentage of hospitalizations with an adverse outcome by diagnostic category and multivariate odds ratio of occurrence compared to unaffected population. Shaded square represents point estimate for odds ratio; lines represent 95% confidence interval.

OR: Odds ratio; PTL: preterm labor; CVD: cerebrovascular disease.

*Due to the small number of events for cerebrovascular disease in NF2 and TS, multivariable models were unreliable and thus an accurate odds ratio could not be determined.

[†]NIS policy prohibits reporting exact numbers or percentages in categories with less than 10 events; for this reason, percentages are written as less than the equivalent of ten over the number of total hospitalizations in that diagnostic category

