Pregnancy and Childbirth in Women With Idiopathic Intracranial Hypertension

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Abstract

Background

Idiopathic intracranial hypertension affects many women of childbearing age. However, the literature is sparse regarding pregnancy outcomes for these women. The goal of this study is to investigate the relationship between pregnancy outcomes in patients with a diagnosis of idiopathic intracranial hypertension.

Methodology

The TriNetX Research Network database was used to query 57 healthcare organizations for patients with idiopathic intracranial hypertension while pregnant (cohort 1) versus those who were pregnant without idiopathic intracranial hypertension (cohort 2). Cohorts were propensity-score matched for confounders related to pregnancy outcomes. The primary outcomes of interest were ectopic or molar pregnancy, cesarean section, abortion, preterm labor, depression, pre-eclampsia or eclampsia, and mortality. Chi-square analysis and logistic analysis were used on categorical variables.

Results

Ectopic/molar pregnancy was seen in 106 (1.75%) versus 117 (1.93%) (odds ratio (OR) 0.904, 95% confidence interval (CI) (0.694, 1.179), p = 0.4572) patients in cohorts 1 and 2, respectively. Cesarean section was seen in 785 (12.94%) versus 886 (14.59%) (OR 0.869, 95% CI (0.784, 0.964), p = 0.0078) patients, abortion in 536 (8.83%) versus 682 (11.24%) (OR 0.765, 95% CI (0.679, 0.862), p < 0.0001), preterm labor in 498 (8.206%) versus 668 (11.01%) (OR 0.723, 95% CI (0.640, 0.816), p < 0.0001), depression in 1,057 (17.42%) versus 1,061 (17.48%) (OR 0.995, 95% CI (0.906, 1.093), p = 0.9238), and pre-eclampsia/eclampsia in 501 (8.26%) versus 492 (8.11%) (OR 1.02, 95% CI (0.896, 1.161), p = 0.7657). Mortality was seen in 68 patients in cohort 1 versus 13 patients in cohort 2 (OR 5.279, 95% CI (2.913, 9.564), p < 0.0001).

Conclusions

This retrospective study examined pregnancy outcomes for pregnant women with a diagnosis of idiopathic intracranial hypertension. Women with idiopathic intracranial hypertension do not have an increase in rates of abortion, ectopic/molar pregnancy, cesarean section, preterm labor, depression, pre-eclampsia or eclampsia, and mortality. Chi-square analysis and logistic analysis were used on categorical variables.

Introduction

Idiopathic intracranial hypertension (IIH), also known as benign intracranial hypertension or pseudotumor cerebri, is a condition of undefined etiology that causes a chronic elevation in the levels of intracranial pressure [1,2]. It is a condition that primarily affects obese women, particularly those who experienced a rapid increase in weight over a short period [3]. This condition primarily presents as chronic diffuse headaches, and patients can experience other symptoms of increased intracranial pressure, such as pulsatile tinnitus and retrobulbar pain, and, left untreated, some patients can develop vision loss [2].

IIH often affects women of childbearing age [4-10]. Of those with IIH, pregnancy has a reported prevalence of 2–12% [4,7,11]. Pregnancy can act as a crucible for IIH as it is often associated with rapid weight gain, increased vasodilation, increased cardiac output, increased blood volume, increased sodium and water retention, increased central venous pressure, and increased Valsalva maneuvers during labor, which, in turn, increase intracranial pressure [4,6,11]. Thus, pregnancy is a unique and high-stakes time that demands careful and effective diagnostic and therapeutic action to best manage the safety of both the mother and the...
fetus. Because current research is limited, and as there are no concrete guidelines to help physicians determine the treatment of IIH in pregnancy, it is necessary to understand associations between pregnancy and IIH [4-6,11]. This study seeks to determine if there is a correlation between IIH and pregnancy complications such as ectopic or molar pregnancy, cesarean section, abortion, preterm labor, depression, pre-eclampsia/eclampsia, and mortality to elucidate if pregnancy is safe for individuals with IIH.

Materials And Methods

This study was designed using a retrospective case-control study model using data obtained from the TriNetX research network. TriNetX is a globally federated health research network that provides access to the electronic health records of patients across many healthcare organizations. This report was run on a set of healthcare organizations grouped into a subnetwork called Research, which includes 57 healthcare organizations. The database was queried using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) and Current Procedural Terminology codes (CPT). Because TriNetX is a federated database, an institutional review board waiver was granted for the use of this database. The use of this database was guided by data in the literature validating this database for similar projects, and the exact details of this research network have already been described [12-14].

The database was queried for patients with a diagnosis of IIH before or up to eight months after the diagnosis of pregnancy and compared against a cohort of pregnant patients without IIH. Cohorts were generated on March 24, 2022. Analysis was performed with several primary endpoints, namely, ectopic or molar pregnancy, cesarean section, abortion, preterm labor, depression, pre-eclampsia or eclampsia, and mortality.

Analysis was performed using propensity score-matched cohorts using a greedy-nearest-neighbor algorithm with a caliper of 0.1 pooled standard deviations. This was to adjust for hypothesized confounders on the relationship between IIH and pregnancy outcomes of interest. The medical information adjusted for included age at the date of pregnancy, sex, race, and comorbidities of hypertension, obesity, hypothyroidism, diabetes, asthma, migraine, epilepsy, prior pregnancy with an abortive outcome, nicotine dependence, coagulation defects, edema, chronic obstructive pulmonary disease, history of spontaneous abortion, thrombocytopenia, history of ectopic pregnancy, antiphospholipid syndrome, prior missed abortion, systemic lupus erythematosus, prior primary inadequate contractions, and prior induced abortions. Hazard ratios were calculated using R’s survival package v3.2-3 and were validated by comparing the output to SAS version 9.4. (SAS Institute Inc. Cary, NC, USA). Chi-square analysis and logistic regression were performed on categorical variables.

Results

Table 1 shows patient count before and after propensity score matching. After propensity matching, 6,069 patients were identified in each cohort.

| Cohort | Patient count before matching | Patient count after matching |
|--------|------------------------------|----------------------------|
| 1: Pregnancy and idiopathic intracranial hypertension | 6,336 | 6,069 |
| 2: Pregnancy and no idiopathic intracranial hypertension | 28,886 | 6,069 |

**TABLE 1: Patient count before and after propensity score matching.**

Table 2 shows the baseline demographics and characteristics of each cohort before propensity score matching, and Table 3 shows the baseline demographics and characteristics after propensity score matching. After matching, the age at index was 28.6 ± 8.7 years and 28.6 ± 9.1 years for cohorts 1 and 2, respectively. Overall, 50.90% versus 51.20% of patients were white, 32.00% versus 32.40% were black or African American, and 16.00% versus 15.40% were of unknown race. Characteristics with less than 10 patients or without significant differences prior to matching were not included in Table 2 and Table 3.
| Code     | Race/Condition                                      | Count | Percentage | p-value | OR    |
|----------|-----------------------------------------------------|-------|------------|---------|-------|
| 2106-3  | White                                               | 3,153 | 50.90%     | 0.223   | 0.017 |
| 2054-5  | Black or African American                           | 1,953 | 31.50%     | <0.001  | 0.122 |
| 2131-1  | Unknown race                                        | 2,554 | 9.70%      | <0.001  | 0.201 |
| 2028-9  | Asian                                               | 45    | 0.70%      | <0.001  | 0.13  |
| 000-008 | Pregnancy with an abortive outcome                  | 358   | 5.80%      | 0.17    | 0.02  |
| 036.80  | Pregnancy with inconclusive fetal viability         | 159   | 2.60%      | 0.533   | 0.009 |
| 003     | Spontaneous abortion                                | 164   | 2.60%      | 0.443   | 0.011 |
| 000     | Ectopic pregnancy                                   | 73    | 1.20%      | 0.013   | 0.037 |
| 002.1   | Missed abortion                                     | 74    | 1.20%      | 0.923   | 0.001 |
| 020     | Hemorrhage in early pregnancy                       | 400   | 6.50%      | <0.001  | 0.075 |
| Z37.1   | Single stillbirth                                   | 11    | 0.20%      | 0.01    | 0.031 |
| I10-116 | Hypertensive diseases                               | 1,129 | 18.20%     | 0.001   | 0.047 |
| E65-E68 | Overweight, obesity, and other hyperalimentation    | 1,986 | 32.10%     | 0.011   | 0.036 |
| 003     | Hypothyroidism                                      | 397   | 6.40%      | 0.003   | 0.043 |
| 008-E13 | Diabetes mellitus                                   | 387   | 6.30%      | <0.001  | 0.192 |
| Z87.891 | Personal history of nicotine dependence             | 355   | 5.70%      | 0.791   | 0.004 |
| F40-F48 | Anxiety, dissociative, stress-related, somatoform, and other nonpsychotic mental disorders | 1,415 | 22.90%     | 0.678   | 0.006 |
| F30-F39 | Mood (affective) disorders                          | 1,351 | 21.80%     | 0.016   | 0.034 |
| M32     | Systemic lupus erythematosus                        | 91    | 1.50%      | 0.235   | 0.016 |
| D65-D69 | Coagulation defects, purpura and other hemorrhagic conditions | 333   | 5.40%      | <0.001  | 0.051 |
| Code | Demographic/diagnosis | Mean ± SD | Patients | Percentage of cohort | P-value | Standard difference |
|------|----------------------|-----------|----------|----------------------|---------|---------------------|
| O10- O16 | Edema, proteinuria, and hypertensive disorders in pregnancy, childbirth, and the puerperium | 28.6 ± 8.7 | 6,069 | 100% | 0.792 | 0.005 |
| F32 | Depressive episodes | 28.6 ± 9.1 | 6,069 | 100% | 0.004 | 0.041 |
| F31 | Bipolar disorder | 68 | 1.10% | 0.012 | 0.033 |
| D68.61 | Antiphospholipid syndrome | 204 | 0.80% | 0.279 | 0.015 |
| D68.62 | Lupus anticoagulant syndrome | 202 | 0.80% | 0.156 | 0.02 |
| D69.6 | Thrombocytopenia, unspecified | 247 | 4.00% | <0.001 | 0.117 |
| G40 | Epilepsy and recurrent seizures | 1,498 | 24.20% | <0.001 | 0.351 |
| G43 | Migraine | 2,896 | 11.00% | | ||
| G44 | Other headache syndromes | 1,815 | 29.30% | <0.001 | 0.308 |
| J44 | Chronic obstructive pulmonary disease | 659 | 2.50% | <0.001 | 0.108 |
| O36.6 | Maternal care for excessive fetal growth | 15 | 0.20% | 0.116 | 0.024 |
| O36.0 | Maternal care for rhesus isoimmunization | 98 | 0.40% | | |

**TABLE 2: Baseline demographics and characteristics before propensity score matching.**
| Code     | Description                                                                 | Count | Percentage | Odds Ratio | p-value |
|----------|------------------------------------------------------------------------------|-------|------------|------------|---------|
| 2028-9  | Asian                                                                        | 45    | 0.70%      | 0.441      | 0.014   |
| O00-08  | Pregnancy with an abortive outcome                                           | 350   | 5.80%      | 0.786      | 0.005   |
| O36.80  | Pregnancy with inconclusive fetal viability                                | 156   | 2.60%      | 0.29       | 0.019   |
| O03     | Spontaneous abortion                                                        | 160   | 2.60%      | 0.822      | 0.004   |
| O00     | Ectopic pregnancy                                                           | 73    | 1.20%      | 0.672      | 0.008   |
| O02.1   | Missed abortion                                                              | 74    | 1.20%      | 0.613      | 0.009   |
| O20     | Hemorrhage in early pregnancy                                               | 400   | 6.60%      | 0.971      | 0.001   |
| Z37.1   | Single stillbirth                                                            | 11    | 0.20%      | 1          | <0.001  |
| I10-16  | Hypertensive diseases                                                        | 1,088 | 17.90%     | 0.08       | 0.032   |
| E65-E68 | Overweight, obesity, and other hyperalimentation                            | 1,906 | 31.90%     | 0.249      | 0.021   |
| E03     | Hypothyroidism                                                              | 388   | 6.40%      | 0.882      | 0.003   |
| E08-E13 | Diabetes mellitus                                                           | 384   | 6.30%      | 0.147      | 0.026   |
| Z87.891 | Personal history of nicotine dependence                                     | 343   | 5.70%      | 0.551      | 0.011   |
| F40-F48 | Anxiety, dissociative, stress-related, somatoform, and other nonpsychotic mental disorders | 1,376 | 22.70%     | 0.069      | 0.033   |
| F30-F39 | Mood (affective) disorders                                                  | 1,321 | 21.80%     | 0.388      | 0.016   |
| M32     | Systemic lupus erythematosus                                                | 86    | 1.40%      | 0.651      | 0.008   |
| D65-D69 | Coagulation defects, purpura, and other hemorrhagic conditions               | 303   | 5.00%      | 0.269      | 0.02    |
| O09-O09 | Supervision of high-risk pregnancy                                          | 1,213 | 20.00%     | 0.124      | 0.028   |
| O10-O16 | Edema, proteinuria, and hypertensive disorders in pregnancy, childbirth, and the puerperium | 612   | 10.10%     | 0.329      | 0.018   |
|        |                                                                              | 1,095 | 18.00%     |            |         |

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TABLE 3: Baseline demographics and characteristics after propensity score matching.

Table 4 shows the outcomes after propensity matching. Ectopic/molar pregnancy was seen in 106 (1.75%) versus 117 (1.93%) (odds ratio (OR) 0.904, 95% confidence interval (CI) (0.694, 1.179), p = 0.4572) patients in cohorts 1 and 2, respectively. Cesarean section was seen in 785 (12.94%) versus 886 (14.59%) (OR 0.869, 95% CI (0.784, 0.964), p = 0.0078) patients, abortion in 536 (8.83%) versus 682 (11.24%) (OR 0.765, 95% CI (0.679, 0.862), p < 0.0001), preterm labor in 498 (8.26%) versus 668 (11.01%) (OR 0.723, 95% CI (0.640, 0.816), p < 0.0001), depression in 1,057 (17.42%) versus 1,061 (17.48%) (OR 0.995, 95% CI (0.906, 1.093), p = 0.9238), and pre-eclampsia/eclampsia in 501 (8.26%) versus 492 (8.11%) (OR 0.1.02, 95% CI (0.896, 1.161), p = 0.7657). Mortality was seen in 68 patients in cohort 1 versus 15 patients in cohort 2 (OR 5.279, 95% CI (2.915, 9.564), p < 0.0001).
| Outcome                     | Cohort 1, n (%) | Cohort 2, n (%) | Odds ratio (95% confidence interval) | P-value |
|-----------------------------|-----------------|-----------------|--------------------------------------|---------|
| Ectopic or molar pregnancy  | 106 (1.75)      | 117 (1.93)      | 0.904 (0.694, 1.179)                 | 0.4572  |
| Cesarean section            | 785 (12.94)     | 886 (14.59)     | 0.869 (0.784, 0.964)                 | 0.0078  |
| Abortion                    | 536 (8.83)      | 682 (11.24)     | 0.765 (0.679, 0.862)                 | <0.0001 |
| Preterm labor               | 498 (8.206)     | 668 (11.01)     | 0.723 (0.640, 0.816)                 | <0.0001 |
| Depression                  | 1,057 (17.42)   | 1,061 (17.48)   | 0.995 (0.906, 1.093)                 | 0.9238  |
| Pre-eclampsia/Eclampsia     | 501 (8.26)      | 492 (8.11)      | 1.02 (0.896, 1.161)                  | 0.7657  |
| Mortality                   | 68 (1.12)       | 13 (0.214)      | 5.279 (2.913, 9.564)                 | <0.0001 |

## TABLE 4: Outcomes after propensity score matching.

### Discussion

The results of this study demonstrate that there is no significant increase in ectopic or molar pregnancy in patients with IIH. Likewise, it shows that cesarean section, abortion, preterm labor, depression, and pre-eclampsia/eclampsia rates are not higher in those with IIH versus those without IIH. However, the mortality rate was significantly higher, albeit low, in the IIH and pregnancy cohort versus those without IIH. Without individualized data, it is difficult to determine the cause of this increase in mortality. Being just above 1%, however, these results demonstrate that pregnancy is well tolerated in patients with IIH.

Although the literature is sparse regarding the management of IIH in pregnancy, several studies have made suggestions on how to best manage this patient population [4-6,11]. The literature has determined that therapeutic abortion is not indicated in this patient population, and the evidence from this study agrees [4,5,7,9,15]. Furthermore, vaginal delivery in IIH has not been associated with worse outcomes, although the mode of delivery is controversial [6,11]. Prolonged active labor has been shown to cause intracranial pressure to rise up to 71 mmHg; nevertheless, there is no evidence to suggest that a cesarean section is a better alternative [4,6]. Currently, the literature suggests that the recommendation for the mode of delivery be made per obstetrics [4,5]. A few studies have also looked at anesthesia during pregnancy and IIH. Reports show that there is no contraindication to spinal or epidural anesthesia [8,16]. Should a cesarean section and anesthesia be required, the goal is to avoid further increases in intracranial pressure, and regional anesthesia may be preferred [8,16].

While rapid weight gain is overall associated with IIH, and weight gain is common in pregnancy, a National Swedish case-control study of IIH demonstrated that risk factors for IIH do not include pregnancy [1,11,17]. Despite weight gain being a risk factor, it is not recommended for pregnant patients to lose or not gain weight. Rather, it is recommended that this patient population avoid excessive weight gain and strictly control their diets to avoid ketosis [4,5,9].

This study does not show an increase in depression among patients with IIH and pregnancy; however, prior literature has shown that IIH alone is associated with increased rates of anxiety and depression. Furthermore, the rates of depression and anxiety during pregnancy correlate with episodes of postpartum depression, and, therefore, it is important to focus on managing this as quickly as possible [4].

Our analysis was not without limitations. The major limitation of this study was that it was retrospective in nature. Furthermore, due to the nature of the database, we were unable to collect patient-level data on specific outcomes. We were unable to report on radiology information. We do not have information on the type of diagnostic test used for confirmation of the disease. We do not have data on fetal outcomes. Although propensity score matching was used for known confounders, unknown confounders may exist. In addition, some misidentification is inevitable in database studies.

### Conclusions

This retrospective study examined pregnancy outcomes for pregnant women with a diagnosis of IIH. It found that women with IIH do not have an increase in rates of abortion, ectopic/molar pregnancy, cesarean section, preterm labor, or depression than women without IIH. The mortality rate was higher in the IIH cohort, but still very low. This study demonstrates that pregnancy is generally well tolerated in the IIH population. Because of a lack of guidelines for its management, it is recommended that pregnant women with IIH do have multi-specialty expertise available.
Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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