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Re-Evaluating the Incidence of Idiopathic Intracranial Hypertension in an Era of Increasing Obesity

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Abstract

Purpose—To re-evaluate the population-based incidence of idiopathic intracranial hypertension (IIH) and determine if it mirrors the rise in obesity.

Design—Retrospective, population-based cohort.

Participants—All residents of Olmsted County, Minnesota, USA, diagnosed with idiopathic intracranial hypertension between January 1, 1990, and December 31, 2014.

Methods—All cases of IIH were identified using the Rochester Epidemiology Project, which is a record-linkage system of medical records for all patient-physician encounters among Olmsted County, Minnesota residents. All medical records were reviewed to confirm a diagnosis of idiopathic intracranial hypertension. The incidence rates of IIH were compared against the incidence of obesity in Minnesota over the same time period.

Main Outcome Measures—Incidence of IIH, lumbar puncture opening pressures, body mass index.

Results—There were 63 new cases of IIH, yielding an overall age- and sex-adjusted annual incidence of 1.8/100,000 (95% CI: 1.3–2.2) between 1990 and 2014. It increased from 1.0/100,000 (1990–2001) to 2.4/100,000 (2002–2014) ($p=0.007$). The incidence of IIH was 3.3/100,000 in women and 0.3/100,000 in men ($p<0.001$). In obese women aged 15 to 44 years,

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the incidence was 22.0/100,000 compared to 6.8/100,000 among all female patients in the same age group. A strong correlation was observed between IHH incidence rates and obesity rates in Minnesota ($R^2=0.70$, $p=0.008$).

Conclusion—The incidence of IHH has increased since 1990, which is highly correlated with the rise in obesity during the same time period.

Keywords

idiopathic intracranial hypertension; pseudotumor cerebri; obesity; incidence

Idiopathic intracranial hypertension (IHH) is a condition of increased intracranial pressure of unknown etiology, often producing papilledema and visual loss.^{1–3} IHH typically occurs in obese women in the childbearing years. The incidence of obesity has been rapidly increasing since the 1970s.⁴ Because obesity is a large risk factor for IHH, the incidence of IHH conceivably could rise in parallel with the current epidemic of obesity, but there have been no studies to evaluate this possibility. Much of the knowledge on the incidence of IHH came from a prior epidemiology study from the Rochester Epidemiology Project (REP), which demonstrated an incidence of 1.0 per 100,000 from 1976 through 1990.⁵ The goal of this study was to re-evaluate the population-based incidence of IHH using the REP and to determine if the incidence of IHH mirrors the large rise in obesity over the past 20 years.

Methods

The medical records of all patients diagnosed in Olmsted County with idiopathic intracranial hypertension, intracranial hypertension, pseudotumor cerebri, or papilledema, from January 1, 1990, through December 31, 2014, were reviewed. Potential subjects were identified using the Rochester Epidemiology Project, a multicenter medical records database designed to capture data on all patient-physician encounters in Olmsted County, Minnesota.^{6, 7} This study was approved by the Institutional Review Board of the Mayo Clinic and the Olmsted Medical Center, Minnesota. It conforms to the requirements of the United States Health Insurance Portability and Accountability Act (HIPAA) and adheres to the tenets of the Declaration of Helsinki.

A total of 427 patients were diagnosed with at least one of the above conditions during the 24-year study period. Patients were classified as having IHH if they met the Modified Dandy criteria, which included signs and symptoms of increased intracranial pressure, no localizing neurologic finding except cranial nerve VI palsies, normal neuroimaging, lumbar puncture opening pressure >250 mm H₂O with normal cerebrospinal fluid constituents, and no other apparent cause. Patients presenting with papilledema and borderline opening pressures (200–250 mm H₂O) were also included in the study.^{3, 8} Patients without papilledema were excluded from this study.

Data on the patients' sex, ethnicity, age at diagnosis, body mass index (BMI), ocular and medical histories, risk factors, presenting signs and symptoms, and treatments were obtained from the medical records. Obesity was defined by a BMI ≥ 30 . Continuous data were presented as a mean and standard deviation, and categorical data were presented as counts

and percentages. Incidence rates and confidence intervals were calculated using population figures in Olmsted County. Age- and sex-adjusted rates were based on the total U.S. white population in 2000. Yearly gender- and age-specific incidence rates were determined by dividing the number of IHH cases within each group by the estimated total Olmsted County resident population. The exact number of obese individuals in Olmsted County was unknown; an estimate of 20% was used based on available statewide rates during the study period. Population figures for 1990, 2000, and 2010 came from the U.S. census data and population; figures for inter-census years were estimated using linear interpolation. Poisson regression models were used to test for trends over time, across age groups, and between genders. Correlation between age- and sex-adjusted IHH incidence and Minnesota obesity rates in two-year categories were estimated using Pearson's correlation coefficient.

Results

From 1990 through 2014, 63 patients were diagnosed in Olmsted County with IHH, 92.1% of who were female (Table 1). Thirty-eight (60.3%) were obese, more than half of whom were morbidly obese (52.6%). BMI was unknown for 17 patients.

The incidence rates of IHH in the Olmsted population are summarized in Table 2. The overall age- and sex-adjusted incidence rate was 1.8/100,000 persons. The IHH incidence increased significantly over the study period from 1.0/100,000 persons between 1990 and 2001 to 2.4/100,000 persons between 2002 and 2014. The incidence of IHH was significantly higher in females than in males, with an overall age-adjusted incidence rate of 3.3/100,000 in females in contrast to 0.3/100,000 in males (p -value<0.001). From 2002 until 2014, the incidence rate had risen to 4.2/100,000 in females and 0.5/100,000 in males.

Table 3 shows the age- and sex-specific incidence rates of IHH in Olmsted County over the study period. The incidence rate peaked at 11.7/100,000 persons for females between the ages of 25 and 34 years, while the rate peaked for males between the ages of 0 and 14 years at 0.8/100,000 persons. Based on Centers for Disease Control (CDC) data for obesity in Minnesota among 15- to 44-year-olds in 2000, the incidence among obese 15- to 44-year-olds was 11.1/100,000 compared to 3.5/100,000 among all patients in the same age group. The incidence rate among obese female patients in this age group was 22.0/100,000 persons compared to 6.8/100,000 persons among all the female study patients in the same age group. Comparing IHH incidence rates to obesity rates in Minnesota from 1990 through 2014 (Figure 1), there was a strong correlation observed between obesity and the age-, sex-, and year-adjusted IHH incidence rates ($R^2=0.70$, $p=0.008$).

Discussion

A prior study utilizing the REP to evaluate the epidemiology of IHH before 1990 found a crude annual incidence of 1.0/100,000 persons and 3.3/100,000 in females 15 to 44 years of age in Olmsted County, Minnesota.⁵ This study has been used to quote the incidence of IHH since it was published in 1993.⁹ Looking at the same patient population, the current study found that the crude annual incidence rate has doubled in Olmsted County, Minnesota, to 2.0/100,000 persons between 1990 and 2014 ($p=0.038$). In addition, within the time period

of the current study, there was a significant rise in the incidence of IIH from the first half of the study at 1.0/100,000 persons to 2.4/100,000 persons in the second half of the study.

In the U.S., the incidence of obesity has been rising from the 1970s until 2014. The prevalence of adulthood obesity, as defined by a BMI of ≥ 30 , was 12.7% from 1976 until 1980, 20.5% from 1988 until 1994, 32.2% from 2003 until 2004, and 34.9% from 2011 until 2012.⁴ Among children, 16.9% were obese as defined by a BMI at or above the 95th percentile.⁴ Obesity in Minnesota in 1990 was <10%, which increased from 15% to 19% in 2000, 20% to 24% in 2010, and 27.6% in 2014 (CDC data).¹⁰ Olmsted County mirrors this trend and now has an adulthood obesity of 27% (CDC data).¹¹ Overall, a strong correlation was found between obesity rates in Minnesota over the study period and the corresponding IIH incidence rates (Figure 1. $R^2=0.70$, $p=0.008$).

Obesity is known to be a large risk factor for IIH. Durcan et al. found that, in Iowa and Louisiana, the incidence of IIH was 19/100,000 among obese women aged 20 to 44 years who were $\geq 20\%$ over ideal weight.⁹ Numerous studies have confirmed that the vast majority of patients with IIH are obese women of childbearing age.^{5, 12, 13} In addition, a recent multicenter case control study demonstrated a “dose-response effect” where higher BMI was associated with a progressively greater risk of IIH.¹⁴ Some studies suggest that environmental factors, such as obesity rates, are responsible for different incidences of IIH in their populations. In Japan, where obesity is less common, the incidence of IIH was found to be only 0.03/100,000,¹⁵ whereas the incidence was reported to be 2.2/100,000 in Libya.¹⁶ Our study confirmed the association between obesity and IIH incidence, where the rate was 22.0/100,000 in obese females aged 15 to 44 years compared to 6.8/100,000 among all female patients in the same age group.

The limitations of the study include the retrospective design, the racial homogeneity of the study population, and incomplete data on obesity rates in the county and state. Given the retrospective nature of this investigation, some patients unavoidably had poor follow-up or incomplete medical records. Secondly, with 90% of the study population identifying themselves as Caucasian, it may be difficult to extrapolate these results to other non-Caucasian populations. Lastly, the exact data on obesity rates in Minnesota could not be found for some of the years within the study period. Olmsted county-specific obesity rates were unavailable during the study years; thus, Minnesota obesity rates were used under the assumption that the obesity rates in Olmsted County were very similar. Despite these limitations, this study yields invaluable results, because it provides a population-based incidence, which directly compares with a prior incidence study also using the Rochester Epidemiology project.⁵ This comparison clearly demonstrates an increase in the incidence of IIH that mirrors the rise in obesity.

In conclusion, this study shows that the incidence rates of IIH and obesity have risen in parallel since 1990. With no sign of obesity rates declining in the U.S., recognizing and treating patients with IIH promptly are, therefore, of increasing importance. Although these patients may only have headaches initially, they can develop severe visual impairment.^{17, 18} Additionally, determining the current incidence of IIH is important, as the annual cost of IIH in the U.S. alone has been estimated to exceed 444 million dollars.¹⁹

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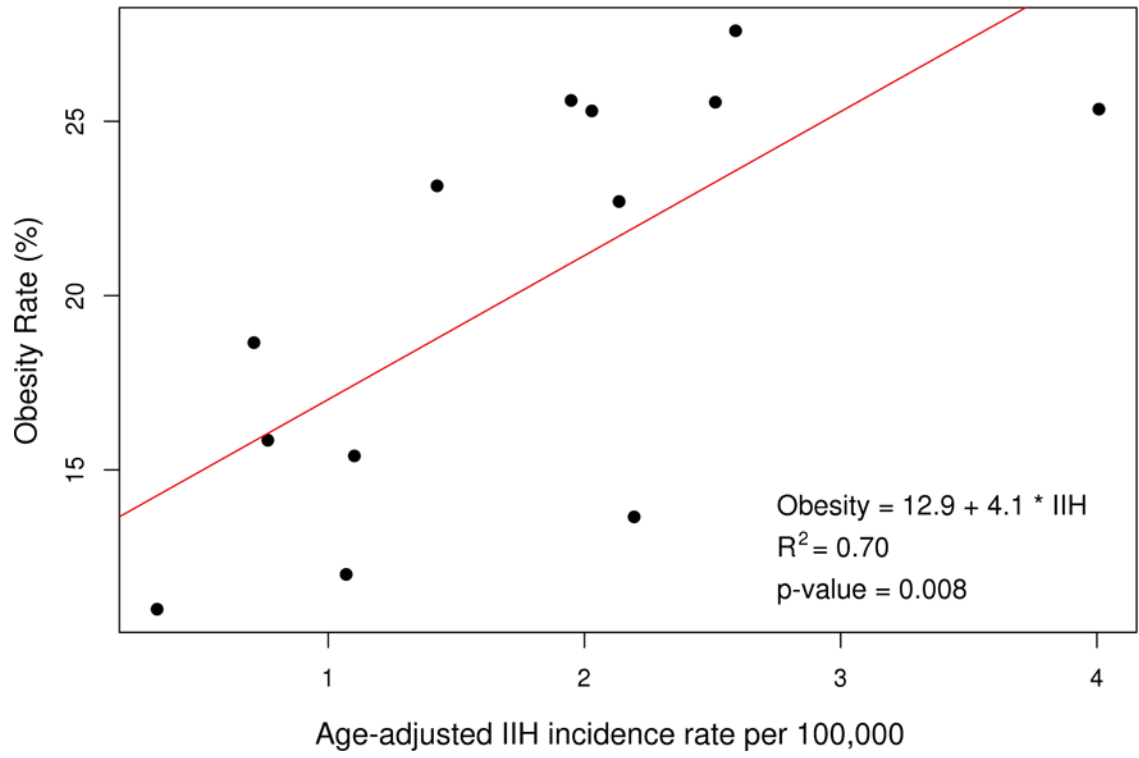


Figure 1.
Correlation between age-adjusted IIH incidence and obesity rates in Minnesota.

Table 1

Historical and clinical characteristics of the 63 patients with IIIH

	N (%)
Sex	
Females	58 (92.1)
Ethnicity	
Caucasian	56 (88.9)
African American	1 (1.6)
Native American	0 (0.0)
Asian	0 (0.0)
Other	4 (6.3)
Unknown	2 (3.2)
Body Mass Index	
<30	8 (12.7)
30–40	18 (28.6)
40	20 (31.7)
Unknown	17

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Table 2

Idiopathic intracranial hypertension incidence rates and BMI by year, sex, and age in Olmsted County from 1990 through 2014

Group	Total N	Incidence Rate (95% CI) Per 100,000 Persons
Years		Age- and Sex- Adjusted Incidence Rate
1990–2014	63	1.759 (1.324, 2.194)
1990–2001	17	1.046 (0.559, 1.575)
2002–2014	46	2.359 (1.676, 3.042)
		<i>p-value: 0.007</i>
Gender 1990–2014		Age-Adjusted Incidence Rate
Males	5	0.290 (0.035, 0.544)
Females	58	3.277 (2.432, 4.121)
		<i>p-value: <0.001</i>
Gender 1990–2001		Age-Adjusted Incidence Rate
Males	0	0.000 (0.000, 0.000)
Females	17	2.129 (1.115, 3.143)
		<i>p-value: <0.001</i>
Gender 2002–2014		Age-Adjusted Incidence Rate
Males	5	0.530 (0.064, 0.997)
Females	41	4.247 (2.945, 5.549)
		<i>p-value: <0.001</i>

Adjusted to the total U.S. white population in 2000. The calculated p-values compare the crude incidence rates. The age-, sex-, and year-adjusted rates are presented to generalize IIH incidence to the U.S. white population.

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Age- and sex-specific average annual incidence rates of IIH in Olmsted County from 1990 through 2014.

Table 3

Group	Female		Male		Total	
	N	Incidence	N	Incidence	N	Incidence
Age (years)						
0-14	4	1.151	3	0.823	7	0.983
15-24	19	9.372	0	0.000	19	4.718
25-34	30	11.673	1	0.396	31	6.084
35-44	4	1.643	0	0.000	4	0.823
45+	1	0.169	1	0.195	2	0.181
All age groups	58	3.534	5	0.318	63	1.961
Age-adjusted ^a	-	3.325	-	0.287	-	1.816
95% CI		2.465 – 4.185		0.033 – 0.542		1.366 – 2.267
Crude Annual Incidence Rate						
Total	58	3.534	5	0.318	63	1.961
Aged 15-44	48	6.826	1	0.144	49	3.508
Obese, aged 15-44 ^b	31	22.041	0	0.000	31	11.097

^a Adjusted to the total U.S. white population in 2000.

^b Accurate data are unavailable on the prevalence of obesity for Olmsted County. These figures assume an obesity rate of 20%, approximated based on CDC data for obesity in Minnesota in 2000. Obesity was defined as body mass index of ≥ 30 .