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EPIDEMIOLOGY AND BURDEN OF HEADACHE

Headache frequency and symptoms of depression as predictors of disability in patients with idiopathic intracranial hypertension

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Idiopathic intracranial hypertension (IIH) is characterized by raised intracranial pressure (ICP) with no established pathogenesis. The disorder is strongly associated with obesity, and most of patients are female of reproductive age. Symptoms of IIH include headaches, often chronic and with associated overuse of symptomatic medications, papilledema and eventually optic nerve atrophy, transient visual obscuration and tinnitus. However, the clinical presentation is variable, and if untreated or treated with excessive delay, IIH can lead to important visual impairment [1]. Diagnosis of IIH requires the following: (a) papilledema; (b) normal neurological examination except cranial nerve abnormalities; (C) neuroimaging study with normal brain parenchyma without hydrocephalus, mass, or structural lesion, and no abnormal meningeal enhancement or venous sinus thrombosis on MRI or MR venography; (d) normal composition of cerebrospinal fluid; (e) raised lumbar puncture opening pressure. If pressure is > 250 mmH2O in lateral decubitus, the diagnosis can formally be appointed. However, the opening ICP threshold of 250 mmH2O is not universally accepted, as many cases would be missed in consideration of large diurnal ICP fluctuations. For this reason, a large trial on IIH proposed less strict criteria and proposed that diagnosis of IIH can be appointed also in those cases with ICP between 200 and 250 mmH2O when associated with compelling clinical and/or MRI findings suggestive of IIH, namely pulse-synchronous tinnitus; abducens nerve palsy; grade II papilledema; no evidence of pseudopapilledema; lateral sinus stenosis or collapse on MRV; partially empty sella with unfolded perioptic nerve CSF spaces [2].

In this observational and cross-sectional study, we enrolled, between April 2013 and November 2017, 81 patients with sign and symptoms suggestive of IIH, on occasion of their participation to an inpatient structured diagnostic program [3]. The program included neurological, neuro-ophthalmologic and psychological examinations, neuroimaging study (including brain MRI and MRI angiography of intracranial vessels), and lumbar puncture with intracranial pressure assessment in the recumbent position. Complete neuro-ophthalmological evaluation including standardized automated perimetry, as functional measurement of optic neuropathy, and spectral domain optical coherence tomography measurements to grade papilledema or optic nerve atrophy. Chronic headache was defined migraine or tension-type headache occurring on 15 or more days/month for more than 3 months, and both headache frequency and average pain intensity were derived from headache diaries. Patients filled in some questionnaires addressing disability (the WHODAS-12), symptoms of depression (the BDI-II). Patients were also examined with regard to the presence of binge eating disorder (BED) according to established diagnostic criteria, and the severity of obesity was addressed in terms of body mass index (BMI).

To address the predictors of disability, we ran a linear regression analysis with target the WHODAS-12 total score. To select predictors, we ran correlations between WHODAS-12 and continuous variables, namely BDI-II total score, number of headaches in the previous 3 months, average pain intensity, BMI, and ICP.

With regard to categorical variables, namely presence of BED, episodic headache, chronic headache, visual impairment, papilledema, and optic neuropathy, those variables that

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Table 1 Main sociodemographic and clinical features and association with WHODAS-12

	N (%); mean ± SD	Correlation and *t* test with WHODAS-12
Female gender	45 (88.2%)	$t = 0.644$
Age	37.4 ± 12.8	$r = -.114$
Headache diagnosis	40 (78.4%)	$t = 2.389$*
Chronic headache diagnosis	20 (39.2%)	$t = 1.953$
Headache frequency/3 months	35.7 ± 35.2	$r = .382$*
Average pain intensity	5.6 ± 2.5	$r = .206$
Visual impairment	34 (66.7%)	$t = 2.053$*
Optic neuropathy	18 (35.3%)	$t = 0.626$
Papilledema	32 (62.7%)	$t = 0.744$
BMI	33.0 ± 6.7	$r = .296$*
BED diagnosis	7 (13.7%)	$t = 0.638$
ICP	333.2 ± 93.3	$r = .085$
BDI-II	11.2 ± 7.7	$r = .506$*
WHODAS-12	22.8 ± 15.2	–

BMI body mass index, *BED* binge eating disorder, *ICP* intracranial pressure, *DBI-II* Beck Depression Inventory, second version, *WHODAS-12* 12-item World Health Organization Disability Assessment Schedule

*$P < .05$

were significantly correlated to the WHODAS-12 and those producing significant differences across groups were retained as candidate predictors for the linear regression analysis. We relied on a backward method (removal criterion, $F \geq 0.10$) so that only the significant independent predictors are included in the final model.

A total of 51 patients, 45 females, mean age 37.4 (SD 12.8) were enrolled. Table 1 reports the main characteristics of participants and the statistic carried out to select the predictors for the regression analysis. Most of the patients were headaches sufferers, with the latter showing significantly higher disability (25.3 ± 14.3 vs. 13.5 ± 15.6) and a significant portion had chronic headache. The level of BMI is indicative of the fact that most of these patients were obese and seven of them (i.e., approximately one out of seven) had comorbidity with BED. Two thirds of the patients had either visual impairment (and reported significantly higher disability, 28.8 ± 14.6 vs.19.8 ± 14.8) or papilledema and one-third had optic neuropathy. The average WHODAS-12 score is suggestive of a relevant disability level in the sample, and the average BDI-II is suggestive of an overall mild level with regard to symptoms of depression.

Headache diagnosis, headache frequency, presence of visual impairment, BMI, and BDI-II scores were retained as predictors for the regression analysis. The final model explained 32% of WHODAS-12 variation and the independent predictors were headache frequency ($\beta = .264$, $P = .038$) and symptoms of depression ($\beta = .434$, $P = .001$).

Disability and impact of IIH on patients' lives have not been systematically evaluated, despite the important burden that is associated to such condition. Patients with IIH, in fact, may report important disability due to several components: presence of headache, visual impairments, obesity, and associated symptoms of depression. All of these variables were associated or had an impact on disability in the patients herein enrolled. Our study, based on a relatively small sample, showed that headache frequency and the severity of depressive symptoms were independent predictors of disability levels in patients with IIH, which were considerably high: in fact, the average score of IIH patients was 22.8 ± 15.2, while that for the Italian general population was 12.9.

What it is interesting to notice here is that the two main predictors of disability are not among the diagnostic criteria for IIH, although their association is known. Treatment for IIH is mostly aimed at reducing ICP, with important benefits on visual function through papilledema reduction and optic nerve atrophy averting, but clinicians should also consider the relevance of headache frequency reduction and mood state improvement to impact on patients' daily lives.

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Compliance with ethical standards

All procedures were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments. Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare that they have no conflict of interest.

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