Turkish Journal of Neurology

Turk J Neurol 2024;30(4):220-224
Doi: 10.55697/tnd.2024.208

ORIGINAL ARTICLE

# Exploring the clinical significance of anemia in idiopathic intracranial hypertension

Nurhan Kaya Tutar, Mehmet Yerturk, Sami Omerhoca, Nilufer Kale

Department of Neurology, Bağcılar Training and Research Hospital, İstanbul, Türkiye

***ABSTRACT***

**Objectives:** This study aimed to explore the clinical significance of anemia in patients with idiopathic intracranial hypertension (IIH).

**Patients and methods:** This retrospective study was performed on 101 consecutive patients with IIH between January 2018 and January 2023. All patients had a complete blood count at the time of admission. Two groups were formed according to the presence of anemia: 32 female patients (mean age: 40±9.6 years; range, 24 to 62 years) with anemia were included in Group 1, and 69 patients (65 females, 4 males; mean age: 40±12.1 years; range 18 to 65 years) without anemia were included Group 2. The groups were analyzed to identify differences in demographic data and visual functions.

**Results:** There was no statistically significant difference in the proportion of female patients (p=0.304), age (p=0.914), and body mass index (29.6±5 *vs.* 31.8±5.7 kg/m$^2$; p=0.070) between Groups 1 and 2. Groups 1 and 2 were not statistically different in terms of visual acuity (0.9±0.2 *vs.* 0.9±0.2 logMAR; p=0.586), retinal nerve fiber layer thickness (128.4±60.8 *vs.* 136.8±64.8 µm; p=0.602), visual field mean deviation (–4.3±4.8 *vs.* –5.1±4.7 dB; p=0.280), and the need for medical treatment (32 of 32 *vs.* 68 of 69; p=0.715).

**Conclusion:** The elucidation of the etiology of IIH is warranted given its propensity to induce severe visual impairment. This study suggested that there was no direct causal relationship between anemia and IIH. Prospective studies in the future could provide further confirmation of our findings

***Keywords:*** Anemia, hematological disorders, idiopathic intracranial hypertension, increased intracranial pressure, pseudotumor cerebri.

Idiopathic intracranial hypertension (IIH) is an uncommon neurological condition characterized by elevated intracranial pressure without any detectable underlying cause and is the idiopathic form of the current umbrella term "pseudotumor cerebri syndrome."[1] This condition predominantly impacts young, overweight females of reproductive age, although it can also affect males and children.[2,3] The most common clinical symptoms are headache, transient visual disturbances, dizziness, pulsating tinnitus, and papilledema, which is the hallmark of IIH.[4] Although the precise mechanisms of the pathophysiology are not fully understood, numerous risk factors have been recognized, including obesity, female sex, hormonal fluctuations, and certain medications such as tetracyclines and corticosteroids.[5,6] Since papilledema, which occurs due to increased intracranial pressure, can lead to permanent vision loss, prompt and appropriate treatment of IIH is essential. In this regard, there are symptomatic treatments with therapeutic agents (acetazolamide and alternative agents, such as furosemide and topiramate) and surgical treatment methods (cerebrospinal fluid [CSF] shunting, venous sinus stenting, and optic nerve fenestration) that can be selected individually for each patient.[7]

Anemia is a common blood disorder characterized by a lack of red blood cells or hemoglobin, resulting in a reduced ability of the blood to carry oxygen. It can have various causes, including nutritional deficiencies (e.g., a lack of

**Correspondence:** Nurhan Kaya Tutar, MD. Bağcılar Eğitim ve Araştırma Hastanesi, Nöroloji Kliniği, 34212 Bağcılar, İstanbul, Türkiye.
**E-mail:** nurhantutar@gmail.com
**Received:** May 14, 2024 **Accepted:** August 15, 2024 **Published online:** December 20, 2024
**Cite this article as:** Kaya Tutar N, Yerturk M, Omerhoca S, Kale N. Exploring the clinical significance of anemia in idiopathic intracranial hypertension. Turk J Neurol 2024;30(4):220-224. doi: 10.55697/tnd.2024.208.

essential nutrients such as iron, vitamin B12, or folic acid), chronic diseases (e.g., chronic kidney disease, cancer, or inflammatory diseases) and genetic diseases (e.g., sickle cell anemia or thalassemia).[8]

The relationship between IIH and anemia has been a topic of interest in recent years. Although several studies suggested a possible link between the two conditions, no definitive underlying mechanism was identified.[9-22] Therefore it is not yet clear whether anemia, which is a common general health problem in society, is a concomitant condition in a rare disease such as IIH or whether it plays a role in the etiology.

Identifying risk factors for IIH is crucial as headaches can severely interfere with activities of daily living and lead to severe vision loss. This study aimed to investigate the possible relationship between anemia and visual function in patients with idiopathic IIH.

## PATIENTS AND METHODS

This retrospective study was performed on 101 patients who were diagnosed with IIH by the neuroophthalmology outpatient clinic at the Bağcılar Training and Research Hospital between January 2018 and January 2023. Friedman et al.'s[23] diagnostic criteria were applied in the diagnosis of IIH. Demographic data, medical history, clinical signs and symptoms on admission, body mass index (BMI), neuroophthalmological examination, and CSF opening pressure measured through lumbar puncture (LP) at the stage of diagnosis, and the type of treatment (acetazolamide or topiramate) after diagnosis (started at any time during the follow-up) were extracted from the hospital data system. A written informed consent was obtained from each patient. The study protocol was approved by the Bağcılar Training and Research Hospital Non-Interventional Clinical Research Ethics Committee (date: 22.12.2023, no: 2023/10/087). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Neuroophthalmological examination parameters performed 24 h before LP included best-corrected visual acuity using the Snellen chart, mean deviation (MD) of the visual field using the Humphrey 30-2 method, and peripapillary retinal nerve fiber layer (RNFL) thickness using optical coherence tomography. The mean RNFL thickness was determined using spectral domain optical coherence tomography (Heidelberg SPECTRALIS OCT; Heidelberg Engineering, Heidelberg, Germany) around the circumference of a circle with a diameter of 3.45 mm in the center of the optic nerve head. The CSF opening pressure was measured in all patients through LP in the lateral decubitus position after intracranial lesions and hydrocephalus were excluded by using brain magnetic resonance imaging. Magnetic resonance venography was performed to exclude cerebral venous thrombosis.

Hemoglobin, hematocrit, mean corpuscular volume, and mean corpuscular hemoglobin concentration results as part of the complete blood count were performed during the diagnostic work-up in our hospital and recorded retrospectively. Anemia was diagnosed based on a hemoglobin concentration <13 g/dL in males and <12 g/dL in nonpregnant females, as defined by the World Health Organization.[24] The patients were evaluated in two groups according to the presence of anemia: 32 female patients (mean age: 40±9.6 years; range, 24 to 62 years) with anemia were included in Group 1, and the remaining 69 nonanemic patients (65 females, 4 males; mean age: 40±12.1 years; range, 18 to 65 years) were included in Group 2. Patients with additional ocular or other systemic diseases and insufficient information on diagnosis at retrospective evaluation were excluded from the study.

### Statistical analysis

Data were analyzed using IBM SPSS version 29.0 software (IBM Corp., Armonk, NY, USA). Frequencies and percentages were reported for categorical data, while the mean, standard deviation, median, minimum, and maximum values were reported for continuous data. Comparisons between groups were performed using the Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. To assess differences in measures between groups while adjusting for BMI effects, Quade nonparametric analysis of covariance was used. A p-value <0.05 was considered statistically significant.

## RESULTS

The groups showed no significant difference in age at the onset of the disease (p=0.914) or in the proportion of female patients (p=0.304). The mean BMI was 29.6±5 in Group 1 and 31.8±5.7 in Group 2, with no significant difference between the groups (p=0.070). Table 1 provides the demographic details of each group.

**TABLE 1**
The demographic characteristics the groups (n=101)

| | Group 1 (n=32) | | | | | Group 2 (n=69) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Variables | n | % | Mean±SD | Median | Min-Max | n | % | Mean±SD | Median | Min-Max | *p* |
| Age (year) | | | 40±9.6 | 39 | 24-62 | | | 40±12.1 | 41 | 18-65 | 0.914* |
| Sex | | | | | | | | | | | 0.304** |
| Male | 0 | 0 | | | | 4 | 5.8 | | | | |
| Female | 32 | 100 | | | | 65 | 94.2 | | | | |
| BMI (kg/m²) | | | 29.6±5 | 29.5 | 21.5-39.7 | | | 31.8±5.7 | 31.6 | 22.5-46 | 0.070* |
| Symptoms | | | | | | | | | | | |
| Headache | 27 | 84.4 | | | | 60 | 87 | | | | 0.762** |
| Pulsatile tinnitus | 18 | 56.3 | | | | 31 | 44.9 | | | | 0.398** |
| TVO | 6 | 18.8 | | | | 8 | 11.6 | | | | 0.363** |
| Blurred vision | 2 | 6.3 | | | | 7 | 10.1 | | | | 0.715** |
| Diplopia | 4 | 12.5 | | | | 4 | 5.8 | | | | 0.259** |
| Nausea | 3 | 9.4 | | | | 4 | 5.8 | | | | 0.676** |
| Vomiting | 3 | 9.4 | | | | 2 | 2.9 | | | | 0.323** |
| Hemoglobin (g/dL) | | | 10.6±1.4 | 11 | 7-11.9 | | | 13.5±1 | 13.3 | 12.1-16.4 | <0.001* |
| Hematocrit (%) | | | 34±3.7 | 34.9 | 24.4-39.5 | | | 40.4±2.6 | 40.2 | 34.1-48.7 | <0.001* |
| MCV (fL) | | | 77.1±9.5 | 77.1 | 57-95.1 | | | 86.4±4.3 | 86.5 | 77.6-101.7 | <0.001* |
| MCHC (g/dL) | | | 31.2±2.2 | 31.4 | 26.5-38.5 | | | 33.3±1.3 | 33.3 | 30.1-39.6 | <0.001* |
| Ferritin | | | 15.3±11.8 | 11.9 | 1.5-52.1 | | | 32.2±26.8 | 26.2 | 2.3-128.4 | <0.001* |
| CSF pressure (cm/$H_2O$) | | | 33.3±7.4 | 32.5 | 20-50 | | | 33.2±8.3 | 32 | 12-60 | 0.888* |
| Medical treatment | 32 | 100 | | | | 68 | 98.6 | | | | 1.000** |
| Acetazolamide | 32 | 100 | | | | 63 | 91.3 | | | | 0.173** |
| Topiramate | 13 | 40.6 | | | | 45 | 65.2 | | | | 0.035** |
| Follow-up period (mo) | | | 31.5±18.6 | 24 | 4-60 | | | 32.4±22.3 | 26 | 2-77 | 0.953* |

SD: Standard deviation; BMI: Body mass index; TVO: Transient visual obscuration; MCV: Mean corpuscular volume; MCHC: Mean corpuscular hemoglobin concentration; CSF: Cerebrospinal fluid; * Mann-Whitney U test; ** Pearson chi-square or Fisher exact test.

**TABLE 2**
Visual functions of the groups (n=101)

| | Group 1 (n=32) | | | Group 2 (n=69) | | | | |
|---|---|---|---|---|---|---|---|---|
| Variables | Mean±SD | Median | Min-Max | Mean±SD | Median | Min-Max | *p* | *p*** |
| Visual acuity LogMAR | 0.9±0.2 | 1 | 0.4-1 | 0.9±0.2 | 1 | 0.2-1 | 0.586* | 0.378 |
| Visual field MD (dB) | –4.3±4.8 | –2.7 | –19-2.9 | –5.1±4.7 | –3.7 | –19.3-2.8 | 0.280* | 0.516 |
| RNFL (µm) | 128.4±60.8 | 111 | 39-261 | 136.8±64.8 | 112 | 41-378 | 0.602* | 0.638 |

SD: Standard deviation; RNFL: Retinal nerve fiber layer; MD: Indicates mean deviation; * Mann-Whitney U-test; ** Quade Nonparametric ANCOVA (adjusted body mass index).

The predominant symptoms in both groups included headache (84.4% in Group 1 *vs.* 87% in Group 2, p=0.762), followed by pulsatile tinnitus (56.3% *vs.* 44.9%, p=0.398), transient visual obscuration (18.8% *vs.* 11.6%, p=0.363), blurred vision (6.3% *vs.* 10.1%, p=0.715), diplopia (12.5% *vs.* 5.8%. p=0.259), nausea (9.4% *vs.* 5.8%, p=0.676), and vomiting (9.4% *vs.* 2.9%, p=0.323). No significant differences were found between the groups concerning initial symptoms, as shown in Table 1.

According to LP results, the mean CSF opening pressure was 33.3±7.4 cm$H_2O$ in Group 1 and 33.2±8.3 cm$H_2O$ in Group 2, with no significant difference (p=0.888; Table 1).

Treatment with topiramate was more prevalent in Group 2, with a statistically significant difference between the groups regarding treatment approaches (p=0.035; Table 1).

Regarding visual function, the mean logMAR visual acuity score was 0.9±0.2 for both groups,

indicating no significant difference (p=0.586). The MD of the visual field was −4.3±4.8 dB in Group 1 and −5.1±4.7 dB in Group 2, without significant differences (p=0.280). The mean RNFL thickness was 128.4±60.8 µm in Group 1 and 136.8±64.8 µm in Group 2. When adjusting for the influence of BMI, no significant difference was observed between the groups in terms of RNFL thickness (p=0.602), as shown in Table 2.

## DISCUSSION

A link between IIH and anemia has been suggested by numerous clinical observations of severe anemia and the subsequent development of papilledema in the literature.[9-16] It was reported that in some of these cases the papilledema resolved only after rapid correction of the anemia.[9-11] Although case reports suggested an association between the two conditions, a small number of further studies were conducted with conflicting results, possibly due to different methodologies. In our study investigating the relationship between IIH and anemia, we divided patients with IIH into those with and without anemia and found that anemia had no effect on demographic characteristics and visual function.

Lin et al.[17] compared patients with IIH and a matched control group and reported that there was no difference in complete blood count values, emphasizing that anemia was not more common in patients with IIH. However, Sverdlichenko et al.[18] showed that the prevalence of anemia was higher in patients with IIH than in neuroophthalmology patients without IIH. Furthermore, according to the results of the meta-analysis by Yu et al.,[19] anemia was significantly more common in patients with IIH than in control patients, and case reports indicated a direct correlation.[9-16]

As in our study, there are few studies that include detailed visual functions in patients with IIH with and without anemia. Ma et al.[20] showed that in patients with IIH and anemia, correcting the anemia in addition to lowering the CSF pressure led to a significant improvement in visual acuity and a shorter duration of disease compared to nonanemic IIH patients. Sverdlichenko et al.[21] reported that among 123 patients with IIH, patients with anemia had poorer visual function at the beginning of the disease and worse visual outcomes than patients without anemia. In contrast, Vosoughi et al.[22] conducted a study on 143 patients with IIH and found no statistical difference between cohorts with and without anemia in terms of variables such as sex, age, BMI, visual acuity, RNFL thickness, MD of visual field, and need for treatment, which is consistent with our findings.

Our study showed that topiramate was more frequently required as an alternative treatment in patients without anemia than in patients with anemia with a statistically significant difference. Although there was no statistically significant difference, MD of visual field and RNFL thickness values of patients without anemia were worse than patients with anemia. In addition, the BMI values of these patients were higher. Considered together with the visual findings, alternative treatment agents may have been required to control IIH at that time.

Idiopathic intracranial hypertension is a heterogeneous disease with a variety of possible contributing factors. While some cases may be linked to specific risk factors or comorbidities, the underlying mechanisms of IIH are not fully understood in many cases. Therefore, it is possible that anemia plays a role in some cases of IIH but not in others, further complicating the attempts to establish a direct link between the two conditions. It is noteworthy that 30% of our patients had anemia. Although IIH mainly affects women of childbearing age, they may be more susceptible to anemia due to blood loss from menstruation, which is consistent with the characteristics of this age group. If both conditions occur in the same person, this could be due to shared risk factors such as obesity or certain medications rather than a direct causal link between anemia and IIH.

This study was limited by the retrospective design and the small number of patients with IIH and anemia.

In conclusion, the elucidation of the etiology of IIH is warranted given its propensity to induce severe visual impairment. In our study, a direct causal relationship between anemia and IIH could not be established. Prospective studies may provide further confirmation of our findings.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Writing, original draft: N.K.T.; Data collection: M.Y., S.O.; Revising the manuscript/study supervision: N.K.I.

**Conflict of Interest:** The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

**Funding:** The authors received no financial support for the research and/or authorship of this article.

## REFERENCES

1. Raoof N, Hoffmann J. Diagnosis and treatment of idiopathic intracranial hypertension. Cephalalgia 2021;41:472-8. doi: 10.1177/0333102421997093.
2. Bruce BB, Kedar S, Van Stavern GP, Monaghan D, Acierno MD, Braswell RA, et al. Idiopathic intracranial hypertension in men. Neurology 2009;72:304-9. doi: 10.1212/01.wnl.0000333254.84120.f5.
3. Gaier ED, Heidary G. Pediatric idiopathic intracranial hypertension. Semin Neurol 2019;39:704-10. doi: 10.1055/s-0039-1698743.
4. Grech O, Mollan SP, Wakerley BR, Alimajstorovic Z, Lavery GG, Sinclair AJ. Emerging themes in idiopathic intracranial hypertension. J Neurol 2020;267:3776-84. doi: 10.1007/s00415-020-10090-4.
5. Markey KA, Mollan SP, Jensen RH, Sinclair AJ. Understanding idiopathic intracranial hypertension: Mechanisms, management, and future directions. Lancet Neurol 2016;15:78-91. doi: 10.1016/S1474-4422(15)00298-7.
6. Chen J, Wall M. Epidemiology and risk factors for idiopathic intracranial hypertension. Int Ophthalmol Clin 2014;54:1-11. doi: 10.1097/IIO.0b013e3182aabf11.
7. Hoffmann J, Mollan SP, Paemeleire K, Lampl C, Jensen RH, Sinclair AJ. European headache federation guideline on idiopathic intracranial hypertension. J Headache Pain 2018;19:93. doi: 10.1186/s10194-018-0919-2.
8. Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Ann N Y Acad Sci 2019;1450:15-31. doi: 10.1111/nyas.14092.
9. Havangi Prakash S, Basavaraju D, Gowda SN. Papilledema and anemia: A rare association. Cureus 2022;14:e25929. doi: 10.7759/cureus.25929.
10. Mollan SP, Ball AK, Sinclair AJ, Madill SA, Clarke CE, Jacks AS, et al. Idiopathic intracranial hypertension associated with iron deficiency anaemia: A lesson for management. Eur Neurol 2009;62:105-8. doi: 10.1159/000222781. b
11. Forman EB, O'Byrne JJ, Capra L, McElnea E, King MD. Idiopathic intracranial hypertension associated with iron-deficiency anaemia. Arch Dis Child 2013;98:418. doi: 10.1136/archdischild-2012-303543.
12. Sim PY, Taribagil P, Woollacott IOC, Rashid S, Kidd DP. Idiopathic intracranial hypertension presenting as iron deficiency anemia: A case report. J Med Case Rep 2021;15:45. doi: 10.1186/s13256-020-02631-2.
13. Henry M, Driscoll MC, Miller M, Chang T, Minniti CP. Pseudotumor cerebri in children with sickle cell disease: A case series. Pediatrics 2004;113:e265-9. doi: 10.1542/peds.113.3.e265.
14. Biousse V, Rucker JC, Vignal C, Crassard I, Katz BJ, Newman NJ. Anemia and papilledema. Am J Ophthalmol 2003;135:437-46. doi: 10.1016/s0002-9394(02)02062-7.
15. Waisberg E, Yu CW, Sverdlichenko I, Micieli JA. New onset severe anemia and fulminant idiopathic intracranial hypertension. Can J Neurol Sci 2022;49:713-5. doi: 10.1017/cjn.2021.203.
16. Terwilliger T, Hall MAK, Galante E. Idiopathic intracranial hypertension: An unusual cause of headache in a patient with sickle cell disease. J Investig Med High Impact Case Rep 2022;10:23247096221140248. doi: 10.1177/23247096221140248.
17. Lin WV, Berry S, Nakawah MO, Sadaka A, Lee AG. Idiopathic intracranial hypertension and anemia: A matched case-control study. J Neuroophthalmol 2020;40:163-8. doi: 10.1097/WNO.0000000000000872.
18. Sverdlichenko I, Yu CW, Margolin E, Micieli JA. Anemia and idiopathic intracranial hypertension: A case-control study. J Neuroophthalmol 2023;43:63-8. doi: 10.1097/WNO.0000000000001664.
19. Yu CW, Waisberg E, Kwok JM, Micieli JA. Anemia and idiopathic intracranial hypertension: A systematic review and meta-analysis. J Neuroophthalmol 2022;42:e78-86. doi: 10.1097/WNO.0000000000001408.
20. Ma Z, Jiang H, Meng C, Cui S, Peng J, Wang J. Idiopathic intracranial hypertension in patients with anemia: A retrospective observational study. PLoS One 2020;15:e0236828. doi: 10.1371/journal.pone.0236828.
21. Sverdlichenko I, Yu CW, Margolin E, Micieli JA. Comparison of idiopathic intracranial hypertension patients with and without anemia. J Neuroophthalmol 2023;43:535-40. doi: 10.1097/WNO.0000000000001715.
22. Vosoughi AR, Sverdlichenko I, Margolin E, Micieli JA. Anemia and idiopathic intracranial hypertension: A prospective study. Can J Ophthalmol 2023:S0008-418200243-0. doi: 10.1016/j.jcjo.2023.07.018.
23. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology 2013;81:1159-65. doi: 10.1212/WNL.0b013e3182a55f17.
24. Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity World Health Organization. Available at: https://www.who.int/vmnis/indicators/haemoglobin/en/ [Accessed: April 12, 2024]