Journal of Health and Rehabilitation Research 2791-156X JHRR

For contributions to JHRR, contact at email: editor@jhrlmc.com

Original Article

Association Between Iron Deficiency Anemia and Chronic Daily Headache

Muhammad Ibrar Saleem[1], Khurram Haqnawaz[1], Shehar Bano Jadoon[1], Salman Khan[1], Jalil Khan[1], Anusha Pervaiz[1], Muhammad Farrukh Habib[2*]

[1]Pak Emirates Military Hospital (PEMH) Rawalpindi
[2]National University of Medical Sciences (NUMS) Rawalpindi
Corresponding Author: Muhammad Farrukh Habib; Email: muhammadfarrukhhabib@gmail.com

Conflict of Interest: None.

Saleem MI., et al. (2023). 3(2): DOI: https://doi.org/10.61919/jhrr.v3i2.194

ABSTRACT

Background: Chronic daily headache (CDH) and iron deficiency anemia (IDA) are prevalent health issues with significant impact on individuals' quality of life. Understanding the relationship between these conditions is essential for developing effective treatment strategies.

Objective: This study aims to investigate the association between iron deficiency anemia and chronic daily headache.

Methods: A case-control study was conducted at Pak Emirates Military Hospital, Rawalpindi, Pakistan, from February to July 2023. The study included 140 patients diagnosed with CDH and 140 age- and sex-matched controls without a history of CDH. Demographic data (age, gender, location, education, marital status) were collected along with clinical characteristics (headache frequency, intensity, duration) and hematological parameters (hemoglobin level, serum ferritin level, red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, platelet count, white blood cell count, hematocrit level, mean corpuscular hemoglobin concentration). Statistical analysis was performed using chi-square tests and ANOVA.

Results: There were no significant differences in demographic characteristics between the CDH and control groups. CDH patients exhibited higher headache frequency (57.14% experienced headaches 10-15 times per month), intensity (64.43% reported NRS score of 5-8), and duration (87.15% reported headache duration of over 4 hours) compared to controls. Hematological analysis revealed significantly lower mean hemoglobin (9.85±2.13 g/dL) and serum ferritin levels (30.72±7.65 ng/mL) in CDH patients compared to controls (13.1±2.70 g/dL and 65.09±12.82 ng/mL, respectively). A significant association between IDA and CDH was established ($p<0.05$).

Conclusion: The study demonstrates a significant association between iron deficiency anemia and chronic daily headache, highlighting the potential role of iron deficiency in the development of CDH.

Keywords: Chronic Daily Headache, Iron Deficiency Anemia, Case-Control Study, Hematological Parameters, Pak Emirates Military Hospital.

INTRODUCTION

Iron deficiency anemia (IDA) and chronic daily headache (CDH) are common health issues that impact millions globally. Iron, crucial for oxygen transport, energy metabolism, and neurotransmitter synthesis, plays a vital role in physiological functions. Insufficient iron levels can lead to both systemic and neurological complications (2). Chronic daily headache, a debilitating condition, is characterized by frequent headaches, with its multifactorial etiology still not fully understood (3).

IDA, a nutritional disorder, is marked by low iron levels in the blood, leading to reduced healthy red blood cell production. This condition is a significant global health concern, affecting people of all ages, particularly women of childbearing age, infants, and the elderly. The most common symptom of IDA is chronic fatigue, often leading to a decline in quality of life (5). Recent studies suggest a possible link between IDA and CDH, with CDH being a form of headache occurring at least 15 times per month for over three months, significantly impairing daily functioning and well-being (7).

The exploration of the potential relationship between iron deficiency anemia and chronic daily headaches is crucial for clinical practice. Identifying a significant correlation could lead to improved diagnostic and treatment strategies for chronic daily headache

Journal of Health and Rehabilitation Research 2791-156X JHRR

(8). Managing iron deficiency anemia through iron supplementation or other means might alleviate the frequency, severity, and burden of chronic daily headache in those affected (9).

The case-control study in question investigated the relationship between IDA and chronic daily headaches. The findings offer valuable insights into the interaction between these conditions, guiding future research and clinical approaches for treating both CDH and IDA. This research aims to enhance understanding of the impact of iron deficiency on the onset and severity of CDH, potentially improving the lives of those suffering from these challenging health conditions.

MATERIAL AND METHODS

In this case-control study conducted at the Pak Emirates Military Hospital in Rawalpindi, Pakistan, from February to July 2023, the relationship between iron deficiency anemia (IDA) and chronic daily headache (CDH) was investigated. The study involved participants who visited the facility during the study period. A total of 140 patients diagnosed with CDH and an equal number of age- and sex-matched controls without a history of CDH were included.

The inclusion criteria for participants were: (1) age 18 years or older, (2) diagnosis of CDH based on the International Classification of Headache Disorders criteria, (3) those who visited the hospital during the study period, (4) patients with complete medical records and necessary information, and (5) those who visited the hospital more than once during the study timeframe. Conversely, the study excluded: (1) individuals under 18 years of age, (2) patients with secondary headache disorders or other known neurological disorders, (3) individuals with a history of head trauma or recent head injury, (4) those with psychiatric disorders or significant psychiatric comorbidities, (5) patients with chronic diseases like cardiovascular or renal diseases, (6) expectant or breastfeeding women, and (7) those unable to provide informed consent or participate in face-to-face interviews and data collection.

Data collection involved face-to-face interviews and reviewing medical records. Demographic characteristics such as age, sex, ethnicity, and socio-demographic variables were gathered. Detailed histories of headache frequency, intensity, duration, and associated symptoms were recorded. Medical histories, including comorbidities, medication use, and previous treatments for CDH, were critically analyzed.

Laboratory measurements included hemoglobin and serum ferritin levels, along with other relevant hematological parameters. Iron deficiency anemia was defined as hemoglobin levels below 10.5 g/dL and serum ferritin levels below 22 microgram/L (10-11). The Numeric Rating Scale (NRS) was used to assess pain intensity, asking participants to rate their headache pain on a scale from 0 (no pain) to 10 (the most excruciating pain imaginable) (12).

Statistical analysis was performed using SPSS 24.0. Descriptive statistics summarized demographic and clinical characteristics. The relationship between IDA and CDH was evaluated using statistical tests such as the chi-square test for categorical variables and ANOVA for continuous variables, depending on the data distribution.

The study acknowledged certain limitations, including the potential inability of the case-control design to establish causality and the sample size possibly affecting the generalizability of findings. Recall bias and reliance on self-reported data were also potential issues, although efforts were made to mitigate these through rigorous data collection and analysis procedures. Ethical approval for the study was granted by the Institutional Review Board, ensuring compliance with ethical standards in research.

RESULTS

In the conducted case-control study at Pak Emirates Military Hospital, demographic characteristics of participants with chronic daily headache (CDH) and controls were analyzed. The mean age of CDH patients was 53.12 years (SD = 10.10 years), compared to 52.87 years (SD = 9.98 years) in the control group. Regarding gender distribution, 69.29% of CDH patients and 67.14% of controls were female. No significant difference was observed in urban-rural distribution or marital status between the two groups, with the majority being married (72.14% in CDH patients and 76.4% in controls).

Clinical characteristics of CDH patients revealed that 57.14% experienced headaches 10-15 times per month, while 27.86% had headaches less than 10 times per month, and 15% experienced them more than 15 times per month. A statistically significant difference was found in headache frequency among CDH patients ($p<0.05$). In terms of headache intensity, 64.43% of CDH patients reported an NRS score of 5 to 8, 19.29% reported a score of less than 5, and 14.28% a score of more than 8. The majority (87.15%) reported headache durations of over 4 hours. These clinical findings indicate a significant variation in headache frequency, intensity, and duration among CDH patients ($p<0.05$).

Clinical signs in CDH patients showed that 85% reported daily headaches, 80% had severe headaches, 65% experienced bilateral headaches, 45% reported nausea, and 35% suffered from photophobia. Additionally, 75% indicated that CDH impaired their daily activities, and 40% faced difficulties in managing their headaches. Furthermore, 70% of the patients found no relief from over-the-counter medications.

Journal of Health and Rehabilitation Research 2791-156X JHRR

Hematological parameters between CDH patients and controls highlighted notable differences. CDH patients had a mean hemoglobin level of 9.85 g/dL (SD = 2.13), significantly lower than the control group's mean of 13.1 g/dL (SD = 2.70) ($p<0.05$). Similarly, mean serum ferritin levels in CDH patients were lower compared to controls ($p<0.05$). Other hematological parameters, such as red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, platelet count, white blood cell count, hematocrit level, and mean corpuscular hemoglobin concentration, showed no significant difference between the groups ($p>0.05$).

Table 1 Demographic Characteristics

S. No	Demographic Characteristic	CDH Patients (n=140)	Control (n=140)	χ2	p-value
1	Age (Mean±SD) years	53.12±10.10	52.87±9.98	0.0069	0.9336
2	Gender n (%)				
	Male	43 (30.71)	46 (32.86)	0.0767	0.7817
	Female	97 (69.29)	94 (67.14)	0.028	0.8670
3	Location n (%)				
	Urban	81 (57.86)	78 (55.71)	0.0361	0.8493
	Rural	59 (42.14)	62 (44.29)	0.0519	0.8197
4	Education n (%)				
	Educated	87 (62.14)	90 (64.29)	0.0312	0.8598
	Uneducated	53 (37.86)	50 (35.71)	0.0639	0.8004
5	Marital Status n (%)				
	Married	101 (72.14)	107 (76.43)	0.0933	0.7526
	Unmarried	31 (22.14)	22 (15.71)	1.2861	0.2567
	Others	08 (5.72)	11 (7.86)	0.4436	0.5053

Table 2 Clinical Characteristics of Participants

S. No	Clinical Characteristics	CDH Patients (n=140)	Frequency (%)	p-value
1	Headache Frequency (per month)			
	<10	39	27.86	0.00001*
	10-15	80	57.14	
	>15	21	15.00	
2	Headache Intensity at NRS Scale			
	<5	27	19.29	0.00001*
	5-8	93	64.43	
	>8	20	14.28	
3	Headache Duration (hours)			
	<2	08	5.71	0.00001*
	2-4	10	7.14	
	>4	122	87.15	
	*Indicates significance (p<0.05)			

Table 3 Comparative Assessment of Hematological Values

S. No	Hematological Parameter	CDH Patients (n=140)	Controls (n=140)	χ2	p-value
1	Hemoglobin Level (Mean±SD) g/dL	9.85±2.13	13.1±2.70	4.221	0.0159*
2	Serum Ferritin Level (Mean±SD) ng/mL	30.72±7.65	65.09±12.82	8.867	0.0029*
3	Red Blood Cell Count (Mean±SD) million/µL	4.1±0.80	4.5±0.91	0.1301	0.7182
4	Mean Corpuscular Volume (Mean±SD) fL	90.10±3.13	91.12±3.40	0.0029	0.9570
5	Mean Corpuscular Hemoglobin (Mean±SD) pg	30.02±2.10	30.87±3.72	0.0126	0.9107
6	Platelet Count (Mean±SD)/ µL	211,000±8300	260,000±9120	2861.8	0.00001*

S. No	Hematological Parameter	CDH Patients (n=140)	Controls (n=140)	χ2	p-value
7	White Blood Cell Count(Mean±SD)/µL	6,500±780	6,200±650	4.3347	0.0373*
8	Hematocrit Level (%)	40.50±3.10	42.34±3.65	0.0346	0.8524
9	Mean Corpuscular Hemoglobin Concentration (Mean±SD) g/dL	32.90±3.76	33.87±3.90	0.0116	0.9141
	*Indicates significance (p<0.05)				

Table 4 Association Between Iron Deficiency Anemia and CDH

S. No	Group	IDA (n=140)	Non-IDA (n=140)	Total (n=280)
1	CDH	108	32	140
2	Controls	19	121	140
3	χ2	45.063		
4	p-value	0.00001*		
5	Level of Significance	Significant		
	*Indicates significance (p<0.05)			

The prevalence of iron deficiency anemia (IDA) was significantly higher in the CDH cohort, with 108 out of 140 patients diagnosed with IDA, compared to 19 out of 140 in the control group. A chi-square test confirmed a significant association between IDA and CDH (p<0.05), indicating a higher likelihood of IDA in patients with CDH. This evidence underscores the significant relationship between IDA and CDH.

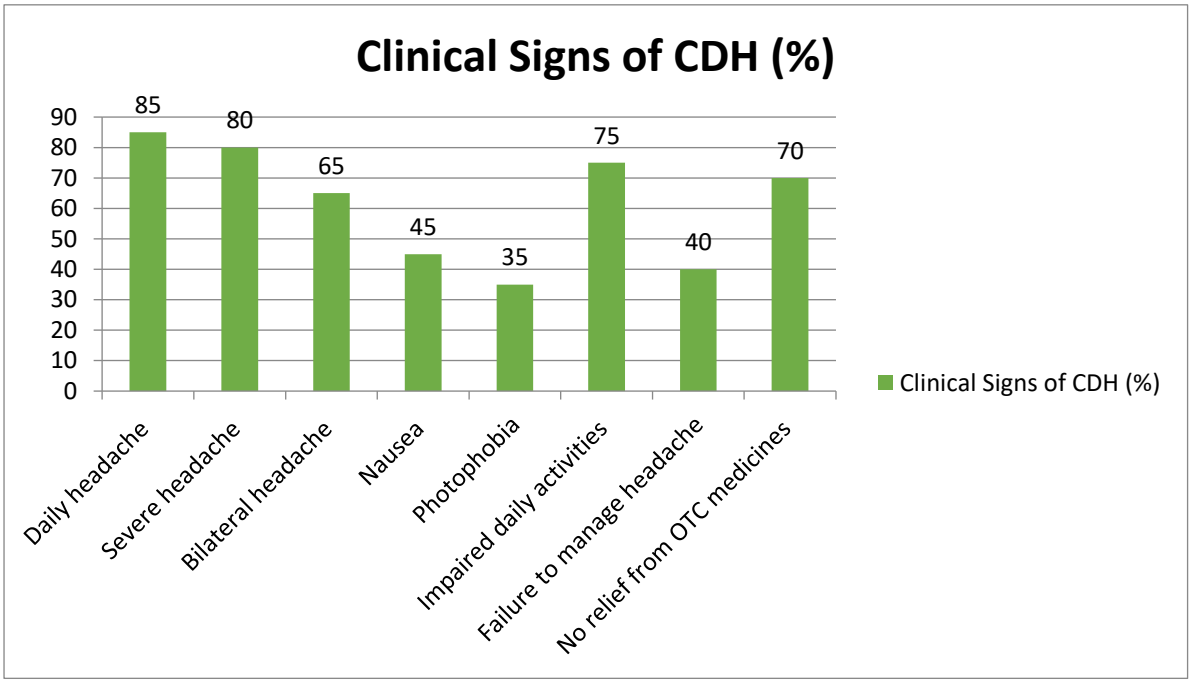

Figure 1 Frequency of clinical signs of CDH patients

DISCUSSION

This case-control study, conducted to explore the relationship between iron deficiency anemia (IDA) and chronic daily headache (CDH), yielded significant insights. The demographic analysis of CDH patients and controls showed no substantial differences in age, gender, location, education level, and marital status. Clinically, CDH patients exhibited more frequent and longer-lasting headaches than the control group, with higher intensity scores on the Numeric Rating Scale (NRS). The symptoms reported by CDH patients, including daily occurrences, severe intensity, and bilateral locations, coupled with additional symptoms like nausea and photophobia, underscored the severity and impact of the disease.

A notable finding was the significantly lower hemoglobin and serum ferritin levels in CDH patients compared to controls, underlining the association between IDA and CDH. This suggests that IDA may contribute to the development of CDH. The study's results align

with previous research, including a 2020 case-control study in India that also found a significant correlation between IDA and CDH (1). Further support comes from studies in neurology journals that recognize the link between IDA and CDH (13-14) and research focusing on women with chronic migraine and tension-type headache, which found a significant relationship between iron deficiency and these headache types (15-16). Iron accumulation in the brain, particularly in regions associated with migraine pathophysiology, and dietary iron's effects on migraine in women of different ages have been noted in other studies (17-18).

A related study conducted at the same hospital in 2018 focusing on female migraine patients found a significant correlation between menstrual abnormalities and IDA in adolescent patients, reinforcing the prevalence of IDA among migraine patients in Pakistan (19-20).

CONCLUSION

In conclusion, this study establishes a strong association between iron deficiency anemia and chronic daily headache, with significant differences in hematological parameters and higher prevalence of IDA in CDH patients. These findings highlight the importance of considering IDA as a potential contributing factor in the evaluation and management of CDH. Further research is required to fully understand the underlying mechanisms and therapeutic implications of this association. The study, however, had limitations, including a small sample size and a need for more extensive, multi-center studies encompassing diverse populations and comorbidities to enhance generalizability.

Acknowledgment is extended to Dr. Farhad and Prof. Muhammad Babar Khan for their valuable contributions to this study, reflecting the collaborative effort in advancing medical research and understanding of these conditions.

REFERENCES

1. Singh RK, Kaushik RM, Goel D, Kaushik R. Association between iron deficiency anemia and chronic daily headache: A case-control study. Cephalalgia. 2023 Feb;43(2):3331024221143540. DOI: 10.1177/03331024221143540
2. Abbaspour N, Hurrell R, Kelishadi R. Review on iron and its importance for human health. J Res Med Sci. 2014 Feb;19(2):164-74.
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3999603/
4. Ahmed F, Parthasarathy R, Khalil M. Chronic daily headaches. Ann Indian Acad Neurol. 2012 Aug;15(Suppl 1):S40-50. doi: 10.4103/0972-2327.100002
5. Miller JL. Iron deficiency anemia: a common and curable disease. Cold Spring Harb Perspect Med. 2013 Jul 1;3(7):a011866. doi: 10.1101/cshperspect.a011866
6. Kumar SB, Arnipalli SR, Mehta P, Carrau S, Ziouzenkova O. Iron Deficiency Anemia: Efficacy and Limitations of Nutritional and Comprehensive Mitigation Strategies. Nutrients. 2022 Jul 20;14(14):2976. DOI: 10.3390/nu14142976
7. Cappellini MD, Musallam KM, Taher AT. Iron deficiency anaemia revisited. J Intern Med. 2020 Feb;287(2):153-170. DOI: 10.1111/joim.13004
8. Murphy C, Hameed S. Chronic Headaches. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022. Bookshelf ID: NBK559083
9. Cocores AN, Monteith TS. Headache as a Neurologic Manifestation of Systemic Disease. Curr Treat Options Neurol. 2022;24(1):17-40. DOI: 10.1007/s11940-022-00704-9
10. Jimenez K, Kulnigg-Dabsch S, Gasche C. Management of Iron Deficiency Anemia. Gastroenterol Hepatol (N Y). 2015 Apr;11(4):241-50. PMCID: PMC4836595; PMID: 27099596.
11. Domellöf M, Hernell O, Dewey KG, Lönnerdal BO, Roberta J. Cohen RJ. The Diagnostic Criteria for Iron Deficiency in Infants Should Be Reevaluated. J Nutr. 2002;132(12):3680-3686. DOI: 10.1093/jn/132.12.3680
12. Choi CW, Cho WR, Park KH, Choi IK, Seo JH, Kim BS, Shin SW, Kim YH, Kim JS, Lee J. The cutoff value of serum ferritin for the diagnosis of iron deficiency in community-residing older persons. Ann Hematol. 2005 Jun;84(6):358-61. DOI: 10.1007/s00277-005-1033-5
13. Krebs EE, Carey TS, Weinberger M. Accuracy of the pain numeric rating scale as a screening test in primary care. J Gen Intern Med. 2007 Oct;22(10):1453-8. DOI: 10.1007/s11606-007-0321-2
14. Aamodt AH, Borch-Iohnsen B, Hagen K, et al. Headache prevalence related to hemoglobin and ferritin. The HUNT Study. Cephalalgia. 2004;24:758–762. DOI: 10.1111/j.1468-2982.2004.00756.x
15. Gür-Özmen S, Karahan-Özcan R. Iron deficiency anemia is associated with menstrual migraine: A case-control study. Pain Med. 2016;17:596–605. DOI: 10.1093/pm/pnv029

Journal of Health and Rehabilitation Research 2791-156X JHRR

16. Sarper N, Zengin E, Cakı Kılıç S, Tugay M, Aydoğan A, Kayabey O. Severe iron deficiency anemia due to late presentation of congenital diaphragmatic hernia in a toddler. Turk J Haematol. 2012 Dec;29(4):430-1. doi: 10.5505/tjh.2012.92609
17. Tayyebi A, Poursadeghfard M, Nazeri M, Pousadeghfard T. Is There Any Correlation between Migraine Attacks and Iron Deficiency Anemia? A Case-Control Study. Int J Hematol Oncol Stem Cell Res. 2019 Jul 1;13(3):164-171. PMCID: PMC6801325
18. Welch KM, Nagesh V, Aurora SK, et al. Periaqueductal gray matter dysfunction in migraine: cause or the burden of illness? Headache. 2001;41(7):629–37. DOI: 10.1046/j.1526-4610.2001.041007629.x
19. Meng SH, Bo ZH, Xin L, Xue WM, Xin KL, Ming FJ, Xia L, Ting LX, Shuang ZY. Association Between Dietary Iron Intake and Serum Ferritin and Severe Headache or Migraine. Front Nutr. 2021;8:685564. DOI: 10.3389/fnut.2021.685564
20. Rashid S, Nawaz HK, Athar HM, Fakhar A,Hakeem F, Manzoor N. Frequency of Iron Deficiency Anemia in Young Females with Migraine. Pak Armed Forces Med J. 2022;72(Suppl-2): S371-374. DOI: https://doi.org/10.51253/pafmj.v72iSUPPL-2.2977
21. Herekar AD, Herekar AA, Ahmad A,Uqaili UL, Ahmed B, Effendi J, et al. The burden of headache disorders in Pakistan: methodology of a population-based nationwide study, and questionnaire validation. J Headache Pain. 2013;14(1):73. DOI: 10.1186/1129-2377-14-73