NeuroRegulation

Diagnostic Yield of Brain Imaging in Headache Patients With Intact Neurological Examination

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Abstract

Background. Many patients presenting with headache complaints are often concerned about the possibility of serious underlying conditions and request brain imaging to rule out ominous pathology. However, brain imaging is costly and carries potential risks for both patients and the healthcare system. **Objective.** This study aims to evaluate the diagnostic value of brain imaging for patients with headaches and intact neurological examination and to identify additional risk factors associated with abnormal imaging results. **Methods.** A retrospective cohort analysis was conducted on 185 patients with primary complaints of headache and normal neurological examinations, assessed at a general neurology clinic over a 4-year period. **Results.** Pathological findings on imaging studies were observed in 9.7% of cases, while 16.2% showed findings of uncertain significance. Patients with pathological or uncertain significance (US) findings are significantly older compared to those with normal results (p = .002 and p < .001, respectively). Male sex is associated with a higher likelihood of US findings (p = .03). Nonthrobbing headaches and the presence of red flags in patient history are linked to pathological findings (p = .001 and p = .002, respectively). The presumption of a secondary headache syndrome before ordering imaging is strongly associated with abnormal imaging results (p < .001 for pathological findings and p < .024 for US findings). **Conclusion.** The decision to perform brain imaging in patients with normal neurological examinations should be individualized based on patient demographics and the presence of nonthrobbing headaches or red flags in the clinical history. A lower threshold for imaging is recommended when secondary headache is suspected.

Keywords: brain imaging; pathological findings; uncertain significance; red flags; incidental findings

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Introduction

Headache is a prevalent neurological disorder affecting people of all ages, with a higher incidence in women (Ahmed, 2012). It is one of the most common medical complaints that makes people seek medical advice. It has a lifetime prevalence of 99% and is one of the most common human afflictions (Silberstein & Lipton, 1996). Primary headaches, including migraine, tension-type, and cluster headaches, account for approximately 98% of cases. In contrast, secondary headaches require urgent attention due to potential life-threatening causes like tumors, infections, vessel abnormalities, or changes in brain pressure (Ahmed, 2012; Kelly et al., 2018).

The third edition of International Headache Criteria (IHCD-3) guides the classification of headache types (Langdon & DiSabella, 2017). Many headache syndromes are diagnosed according to clinical criteria rather than brain imaging findings or other investigations. Brain imaging is sometimes needed to exclude ominous diagnoses or support other differential diagnoses. Current guidelines discourage routine diagnostic tests in the absence of red flags, and the patient has no focal neurological deficit (Kelly et al., 2018). Brain tumors, though uncommon, can cause headaches and warrant investigation if red flags are present (Kirby & Purdy, 2014). Proper diagnosis and management of headaches are crucial for improving patients' quality of life and reducing healthcare costs (Ahmed, 2012).

Brain magnetic resonance imaging (MRI) in headache patients has limited diagnostic value, with significant findings detected in only 4.9%–8.86% of cases (Jang et al., 2019; Yüksel et al., 2022). However, certain factors increase the likelihood of significant findings, including age over 65, acute onset of headache, and the presence of red flag in clinical history (Kaur et al., 2019; Yüksel et al., 2022). Common incidental findings include white matter abnormalities, arachnoid cysts, and enlarged perivascular spaces (Gurkas et al., 2017; Toker et al., 2023). Neuroimaging in such conditions is frequently requested for medicolegal documentation or reassurance, rather than based on clinical necessity, as its yield in patients with normal neurological examinations is equivalent to that of the general asymptomatic population (Mullally & Hall, 2018). Nevertheless, MRI remains a valuable tool for ruling out secondary causes of headaches (Jang et al., 2019). Given its limited diagnostic utility in the absence of concerning features, neuroimaging should be reserved for headache patients who present with red flags (Jang et al., 2019; Kaur et al., 2019). The MRI is the modality of choice for the brain tissue as it gives more detailed information, and there is no risk of radiation exposure (Kamtchum-Tatuene et al., 2020).

On the other hand, neuroimaging in headache patients may detect nonsignificant findings. Those findings may be incidental and unrelated to headache complaints or normal variants that can present in many normal people, leading to more consultations and more investigations to prove their nonrelevance or nonsignificance (Graf et al., 2010; Moodley & I Bhigjee, 2022). The detection of these incidental findings can increase stress and obsession about having a threatening disease and raise another dilemma about proving their significance or nonsignificance. For this reason, sometimes doing imaging studies in such conditions can do more harm than benefit, increasing healthcare costs and extending the waiting queues. The current guidelines recommend against routine neuroimaging in patients with normal neurological examinations; individual assessment is crucial (Kamtchum-Tatuene et al., 2020; Young et al., 2018).

This study aims to detect the frequency of abnormal neuroimaging in headache patients with normal neurological examination and to identify risk factors for abnormal findings using subgroup analysis.

Materials and Methods

Methods

This study is a retrospective cohort analysis conducted at a general neurology clinic in Mosul, Nineveh, Iraq. It included patients who presented with headache as their primary complaint and had a normal neurological examination. The data were extracted from electronic medical records spanning from October 2019 to January 2025.

Inclusion Criteria

Patients aged 4 years and older were eligible for inclusion if they presented with a chief complaint of headache, had no focal neurological deficits on examination, and underwent neuroimaging (MRI or computed tomography [CT]) following clinical evaluation.

Exclusion Criteria

Patients were excluded if they met any of the following conditions:

a) Headache was a secondary or accompanying symptom rather than the primary complaint.
b) Presence of a focal neurological sign or meningeal irritation on examination.
c) Neuroimaging was not performed.
d) Medical record was incomplete or lacked essential diagnostic or demographic data.

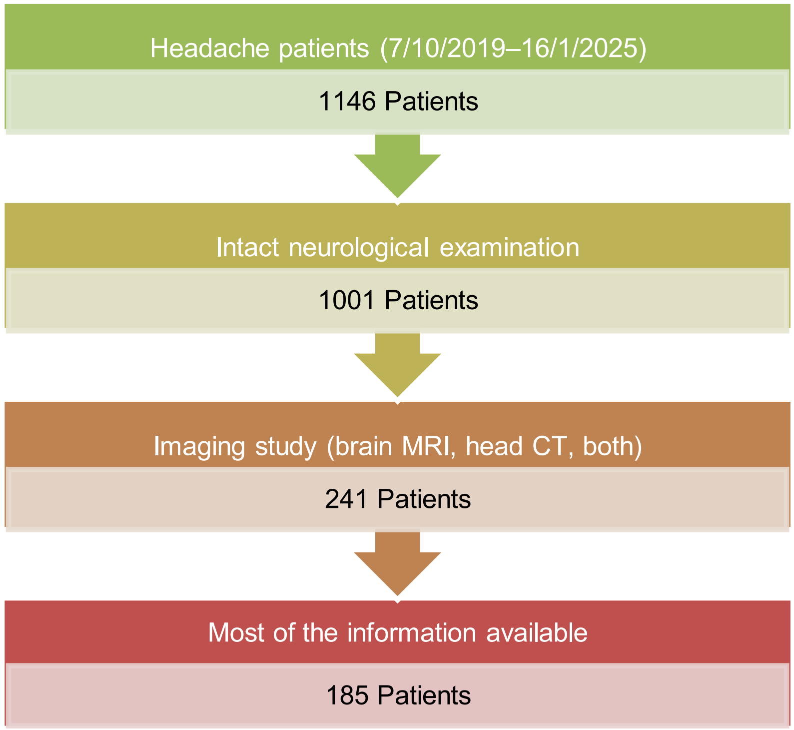
See Figure 1 for a detailed flowchart of patient selection.

The primary objective of the study was to evaluate the diagnostic yield of neuroimaging in patients presenting with headache and a normal neurological examination. The secondary objective was to identify clinical and demographic risk factors associated with abnormal imaging findings through subgroup analysis.

Ethical Approval

All participants involved in this study provided informed consent prior to their participation. The study was approved by the Mosul medical college ethics committee (Ref. No. UOM/COM/MREC/23-24/JUL9) and participants were fully informed about the purpose, procedures, and potential risks associated with their involvement.

Figure 1. *Flow Chart of Patients Gathering.*



Data Collection

Patient records were retrieved using Microsoft Access 2010, the digital medical record system utilized in the neurology clinic. Data were filtered using predefined criteria on the main interface to identify eligible cases. A total of 185 patients met the inclusion criteria and were enrolled in the study.

The collected data included patient demographics (age, sex), duration of headache (categorized into three groups: acute [days], subacute [months], and chronic [years]; Gonzalez-Martinez et al., 2024), history of present illness, presence of red flag symptoms, and relevant past medical, surgical, drug, social, and family histories. All patients underwent general and neurological examinations, the findings of which were documented.

Details of investigations, including neuroimaging studies (MRI or CT of the brain), and final clinical diagnoses were entered into Microsoft Excel 2010 for analysis.

Neuroimaging findings were classified into three categories:

a) ***Normal.*** No significant abnormalities reported by the radiologist or observed by the neurologist upon review.
b) ***Pathological.*** Findings deemed relevant to the patient's headache and requiring specific medical or surgical intervention.
c) ***Findings of US.*** Imaging abnormalities that may or may not be related to the headache and do not necessitate immediate or specific treatment (white spots of brain [Longstreth et al., 1996], arachnoid cyst [Al-Holou et al., 2013] and brain atrophy [Sargent & Lawson, 1980]).

Data Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables were assessed using Chi-square tests applied to 2×2 and 3×3 contingency tables. A *p*-value of <.05 was considered statistically significant for 2×2 comparisons, while a Bonferroni-corrected *p*-value threshold of <.0056 was applied for 3×3 comparisons to account for multiple testing.

For continuous variables, one-way analysis of variance (ANOVA) was used to compare means among groups, following verification of normal distribution using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Post hoc analysis was conducted using the Tukey Honest Significant Difference (HSD) test when appropriate.

The manuscript was prepared in accordance with the CONSORT (Consolidated Standards of Reporting Trials) guidelines (Moher et al., 2010).

Results

A total of 185 consecutive patients presenting with headache as their primary complaint and exhibiting normal neurological examinations were evaluated and included in the study (Figure 1). Among the cohort, 34.1% were male.

The duration of headache symptoms was categorized chronologically (Table 1):

- Acute (days): 38.9%
- Subacute (months): 20.0%
- Chronic (years): 41.1%

Red flag features in the clinical history (Table 2) were identified in 37.7% of patients. Additionally, 27% of patients exhibited instability in vital signs during examination (e.g., abnormal blood pressure, fever, or abnormal pulse), while 5% had abnormal general physical examination findings (e.g., anemia, jaundice, etc.).

Neuroimaging was ordered based on the presence of red flags or per patient request to alleviate anxiety. MRI was the preferred imaging modality, performed in 71.4% of cases, compared to 30.8% who underwent head CT. Some patients underwent both.

Patients with pathological imaging findings and those with findings of uncertain significance were significantly older than patients with normal imaging results (p = .002 and p < .001, respectively; Table 4).

A nonthrobbing headache quality and the presence of red flags in the history were both strongly associated with pathological imaging findings (p = .001 and p = .002, respectively).

Presumptive diagnosis of a secondary headache syndrome was significantly associated with both pathological findings and findings of US (p < .001 and p = .024, respectively). Additionally, male sex was significantly associated with the presence of findings of US (p = .03).

No statistically significant associations were found between imaging findings and either vital sign instability or abnormal general examination findings (p > .05 in all cases; Table 5).

Table 1
Frequency of Categorical Data

Variable	Frequency	Percentage
Sex (Male)	63	34.1%
Duration		
Days	72	38.9%
Months	37	20.0%
Years	76	41.1%
Red flags (Yes)	69	37.3%
Stability (No)	49	26.5%
General examination (abnormal)	10	5.4%
Type of imaging		
MRI	128	69.2%
CT	53	28.6%
Both	4	2.2%
Diagnosis (presumed secondary)	27	14.6%
Imaging finding		
Normal	137	74.1%
Findings of uncertain significance	30	16.2%
Pathological	18	9.7%

Table 2
Red Flags in History

1. Childhood-onset	15. Dysphasia
2. Old age >65 years	16. Numb chin
3. Acute in onset	17. Fever
4. Postcoital	18. Weight loss
5. Thunderclap in character	19. Flu-like illness
6. Cluster in character	20. Post-COVID-19
7. Loss of consciousness	21. No response to treatment
8. Forgetfulness	22. Changing character
9. Facial numbness	23. History of familial dyslipidemia
10. Facial weakness	24. History of benign intracranial hypertension
11. Facial pain	25. History of breast cancer
12. Deafness or tinnitus	26. History of chronic kidney disease
13. Sided numbness	27. History of recent trauma to head
14. Sided weakness	28. History of hypertensive crisis

Table 3
Pathological Findings and Findings of Uncertain Significance (US) in Headache Cohort

	Pathological findings	No.		Findings of US	No.
1.	Ischemic infarctions	8	1.	White spots of the brain	25
2.	Intracerebral hemorrhage	2	2.	Brain atrophy	3
3.	Cerebellopontine angle ependymoma	1	3.	Arachnoid cyst	2
4.	Maxillary sinusitis, pan sinusitis	2			
5.	Parasagittal lesion (AVM or tumor)	2			
6.	Internal carotid artery aneurysm	1			
7.	CSF leakage from anterior cranial fossa to Right nasal sinus	1			
8.	Linear skull fracture	1			

Table 4
Association Between Age and Imaging Findings Using One-Way ANOVA Test

	(I) Findings	Mean Age (Year)	*SD*	(J) Findings	Sig.(I–J)
Tukey* HSD	Normal	37.5	15.8	Findings of US	**< .001**
				Pathological	**.002**
	Findings of US	58.7	16.3	Normal	**< .000**
				Pathological	.239
	Pathological	51.1	14.2	Normal	**.002**
				Findings of US	.239

* = Tukey HSD test is used for post hoc multiple comparisons after assuring normal distribution of data (Kolmogorov–Smirnov and Shapiro–Wilk).

Table 5
Relation Between Clinicodemographic Features and Imaging Findings Using Chi-Square Tests 2x2 Table

Clinical & demographic features		Imaging findings		
		Normal	**Pathological**	**Findings of US**
Sex	Male	40	8	15
	Female	97	10	15
	OR	Ref.	1.9	2.4
	95%CI		0.71–5.3	1.08–5.4
	p-value		.19	**.03**
Headache characteristics	Throbbing	85	4	15
	Nonthrobbing	52	14	15
	OR	Ref.	5.8	1.6
	95%CI		1.8–18.7	0.7–3.6
	p-value		**.001**	.22
Red flags	No	90	5	21
	Yes	47	13	9
	OR	Ref.	4.9	0.82
	95% CI		1.7–14.8	0.39–1.9
	p-value		**.002**	.65
General examination	Normal	131	17	26
	Abnormal	5	1	4
	OR	Ref.	1.5	4
	95% CI		0.17–13.9	1–16
	p-value		.53*	.06*
Vital signs	Stable	92	12	19
	Unstable	33	6	10
	OR	Ref.	1.3	1.47
	95%CI		0.48–4.01	0.62–3.5
	p-value		.57*	.38
Preliminary diagnosis	Presumed 1º	122	9	22
	Presumed 2º	15	9	18
	OR		8.1	2.9
	95%CI		2.8–23.67	1.12–7.81
	p-value		**<.001***	**.037***

OR = odd ratio, CI = confidence interval, Ref. = Reference, 1º = primary headache, 2º = secondary headache, * = Fisher-exact test is used.

When evaluating the relationship between imaging findings and either the duration of illness (acute, subacute, chronic) or type of imaging modality (MRI, CT, or both) using 3×3 contingency tables, no statistically significant associations were detected after Bonferroni correction (Table 6).

Table 6
Relation Between Durations of Illnesses and Imaging Modalities From One Perspective and Imaging Findings From Another Perspective Using 3x3 Contingency Table Chi-Square Test

		Imaging findings		
		Normal (*p*-value)*	Pathological (*p*-value)	Finding of US (*p*-value)
Durations	**Days**	45 (.08)	12 (.18)	15 (.74)
	Months	31 (.69)	3 (.1)	3 (.69)
	Years	61 (.63)	3 (.3)	12 (1)
Imaging modality	**Brain** MRI**	89 (.35)	11 (.96)	28 (.04)
	Head CT	45 (.35)	6 (.99)	2 (.08)
	Both	3 (1)	1 (.91)	0 (.94)

* All *p*-values are not significant (significant *p* value after Bonferroni correction ≤ .0056). ** MRI = magnetic resonance imaging, CT = computed tomography.

Discussion

In Iraq, the diagnostic yield of neuroimaging in patients presenting with headache and a normal neurological examination has not been clearly established. In the present study, pathological findings were identified in 9.7% of patients, while findings of US were observed in 16.2%. These results are consistent with previous studies by Kamtchun-Tatuene et al. (2020) and Moodley & I Bhigjee (2022), which reported similar frequencies of abnormal imaging findings in comparable patient populations.

Clinically significant findings—defined as abnormalities that could potentially alter treatment decisions—were identified in approximately 10% of patients in our cohort. This proportion aligns with findings reported by Jang et al. (8.86%; 2019) and Kamtchun-Tatuene et al. (17.5%; 2020). However, these results contrast with those of Sempere et al. (2005), who reported a markedly lower prevalence of significant intracranial abnormalities (0.9%) in a cohort of patients with nonacute headaches. The observed discrepancies may be attributed to differences in study design, inclusion criteria, and the potential for missed cases in cohorts with less stringent data collection methods.

The white spots of the brain are more prevalent in migraineurs, tension-type headache, and middle-age patients, but their relation to headache is not clearly understood (Honningsvåg et al., 2018; Schramm et al., 2024). On the other hand, arachnoid cysts are often asymptomatic but larger cysts may cause headache, seizure or focal neurological deficit (Cherian et al., 2014). Brain atrophy has been also linked to headache, especially in migraineurs, by unknown mechanism (Devianne et al., 2022). We have assumed "finding of uncertain significance (US)" for these constellations that have been previously reported as "incidental findings" or "findings that do not change treatment plans" (Moodley & I Bhigjee, 2022).

Patients with pathological findings (51.1 years ± 14.2) and findings of US (58.7 years ± 16.3) are considerably older than those with normal findings (37.5 years ± 15.8). Kim et al. (2020) recognized that age ≥50 years at headache onset was related to incidental findings, while age ≥40 years was linked to pathological results. Similarly, Lemmens et al. (2021) emphasized that headache onset after age 50 should be considered a clinical warning sign.

A noteworthy finding in this cohort is the significant association between male sex and the presence of findings of uncertain significance. Khalid and Salih (2024) also demonstrated a higher rate of abnormal MRI findings among male patients compared to females. These studies emphasize the importance of sociodemographic factors in selecting headache patients for imaging techniques.

The relationship between headache duration and imaging abnormalities is complex. While some studies indicate that abnormal imaging findings increase with age and are more common in males, they appear largely independent of symptom duration (Sun & Cao, 2011). In pediatric populations, however, headache duration of less than 6 months has been linked to abnormal imaging (Medina et al., 1997), while other studies found that chronic headaches are more likely to yield abnormal findings (Rai, 2016). In our study, no significant association was found between symptom duration and imaging abnormalities.

The throbbing quality of headache, often characteristic of migraine (Hernandez et al., 2024), was inversely associated with pathological imaging findings in this cohort. Specifically, nonthrobbing headaches were significantly more frequent among patients with pathological imaging but not among those with US findings. These findings underscore the need for further investigation into the pathophysiological relevance of headache quality in differentiating primary from secondary headache syndromes.

The utility of red flag symptoms in selecting patients for imaging remains controversial. While some authors argue that three or more red flags are necessary to predict abnormal imaging (Manoyana et al., 2022; Sobri et al., 2003), others report low diagnostic yield even in their presence (Tsze et al., 2019; Young et al., 2018). In our cohort, red flags were significantly associated with abnormal imaging findings, supporting their value in clinical decision-making.

Notably, abnormalities in general physical examination (e.g., pallor, jaundice, cyanosis) and vital sign instability (e.g., hypertension, fever, irregular pulse) were not predictive of abnormal imaging outcomes. Although hypertensive encephalopathy has been linked to cytotoxic edema on imaging, this is likely due to loss of cerebral autoregulation rather than ischemia (Schwartz et al., 1992). To our knowledge, this aspect remains underreported in the literature and merits further investigation.

Comparative studies on imaging modalities in headache patients show mixed results. CT is superior for detecting bony lesions, skull base pathology, and acute hemorrhages, whereas MRI provides better resolution for parenchymal abnormalities (Agarwal & Kanekar, 2022; Lemmens et al., 2021; McCullagh et al., 2022). In our study, no statistically significant advantage was observed for either MRI or CT—or their combination—in detecting clinically relevant abnormalities in an outpatient setting. Therefore, imaging choice should be guided by specific clinical features, suspected pathology, and urgency of assessment.

The strength of this study lies in the use of a digital medical database to minimize interpretive bias and the application of robust inclusion and exclusion criteria. Subgroup analysis provided valuable insights into underexplored aspects of headache imaging. However, several limitations must be acknowledged. The single-center design may limit generalizability, and referral bias may have led to an overestimation of abnormal findings, as many excluded patients with presumed benign headaches did not undergo imaging. Additionally, the retrospective nature of the study limits control over confounding variables and introduces record bias.

To the best of our knowledge, this is the first Iraqi cohort study to evaluate the frequency and nature of abnormal imaging findings in headache patients with normal neurological examinations, and to identify associated demographic and clinical predictors.

Conclusion

The decision to perform neuroimaging in headache patients with a normal neurological examination should be individualized, taking into account demographic characteristics, headache features, and clinical history. As an alternative or complement, neuroregulation and neuromodulation techniques, including neurofeedback and noninvasive stimulation, may offer more targeted and cost-effective strategies for managing this population. The presence of red flag symptoms, older age, and nonthrobbing headache quality were all associated with a higher likelihood of abnormal imaging. Male sex was linked to findings of uncertain significance. Importantly, physical exam abnormalities and vital sign instability were not predictive of imaging abnormalities.

Careful application of clinical guidelines and judicious use of imaging may reduce unnecessary investigations, lower healthcare costs, and shorten waiting times. Further prospective, multicenter studies with longer follow-up periods are warranted to better understand the clinical significance of incidental imaging findings and to refine the predictive value of specific headache features.

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