

Common diagnoses and factors associated with abnormal neuroimaging in headache patients in the emergency department

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ABSTRACT

الأهداف: تحديد أسباب الصداع لدى المرضى الذين قدموا إلى قسم الطوارئ وخضعوا لتصوير الأعصاب، وتحديد السمات السريرية المرتبطة بالتصوير العصبي غير الطبيعي.

المنهجية: اخترنا المرضى بأثر رجعي من قاعدة بيانات خلال الفترة من يونيو 2015م ومايو 2019م. اشتملت الدراسة على المرضى الذين لديهم تصوير عصبي مطلوب من ED بشكل رئيسي للصداع. قيمنا الارتباط بين الخصائص السريرية والتصوير العصبي غير الطبيعي.

النتائج: اشتملت الدراسة على 329 مريضاً (33.4% رجال و 66.6% نساء). كان متوسط العمر (SD) 39.7 (18.4) سنة. أبلغنا عن العلامات العصبية في 43.8% من المرضى، وطلب التصوير المقطعي للرأس في 79.6%، والتصوير بالرنين المغناطيسي في 77.5%، وكلاهما في 57.1%. تم الإبلاغ عن تصوير عصبي غير طبيعي في 31.9%. كانت التشخيصات الأكثر شيوعاً هي اضطرابات الصداع الثانوية (48.9%)، تليها اضطرابات الصداع الأولية (16.4%). أما البقية فكانت من صداع غير محدد (35%). كانت المتغيرات المرتبطة بالتصوير العصبي غير الطبيعي هي ظهور الصداع شهر واحد (OR=3.37، فترة الثقة=1.47-7.70) ($p=0.004$) ووجود علامة عصبية غير طبيعية (OR=3.60، فترة الثقة=1.89-6.83) ($p<0.001$).

الخلاصة: اضطرابات الصداع الثانوية شائعة في المرضى الذين يخضعون لتصوير الأعصاب في الطوارئ. أولئك الذين لديهم علامة عصبية وظهور صداع حديثاً هم أكثر عرضة للتصوير العصبي غير الطبيعي.

Objectives: To determine causes of headaches in patients who presented to the emergency department (ED) and underwent neuroimaging, and to determine the clinical features associated with abnormal neuroimaging.

Methods: Patients were retrospectively selected from a database between June, 2015 and May, 2019. Patients were included if they had neuroimaging requested

from the ED mainly for headache. Associations between clinical characteristics and abnormal neuroimaging were assessed.

Results: We included 329 patients (33.4% men, 66.6% women). The mean (SD) age was 39.7 (18.4) years. Neurological signs were reported in 43.8% of the patients, head-computed tomography was requested in 79.6%, magnetic resonance imaging in 77.5%, and both in 57.1%. Abnormal neuroimaging was reported in 31.9%. The most common reported diagnoses were secondary headache disorders (48.9%), followed by primary headache disorders (16.4%). The remainder were nonspecific-headaches (35%). Variables associated with abnormal neuroimaging were headache onset ≤ 1 month (OR 3.37, CI 1.47–7.70, $p=0.004$), and presence of an abnormal neurological sign (OR 3.60, CI 1.89–6.83, $p<0.001$).

Conclusion: Secondary headache disorders are common in patients who undergo neuroimaging in the ED. Those who have a neurological sign and recent onset of headache are more likely to have abnormal neuroimaging.

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The prevalence and burden of primary headaches is large worldwide.^{1,2} In Saudi Arabia, the prevalence of both migraine and tension-type headaches has been

reported to be higher compared to the global average.³ A cross-sectional study from the 13 regions of Saudi Arabia included 2316 participants that were phone-interviewed, and reported that the adjusted one-year prevalence of all headache types was 65.8%, and that of migraine 25%.³ In the Aseer region, a questionnaire-based study of 1123 participants reported the prevalence of migraine and non-migraine headaches to be 12.3% and 74.2%, respectively.⁴ Another local study with more than 4,000 participants reported a prevalence of all headache types of 84%, with 24% of the participants having had a migraine.⁵

Headache is one of the most common presenting symptoms to the emergency department (ED).⁶ In the United States (U.S), headache accounts for almost 2% of all visits to the ED every year.⁶ However, headache disorders managed in the ED are quite different from those prevalent in the community.⁷ Secondary headache disorders should be identified and treated promptly to avoid dire consequences. The third edition of the International Classification of Headache Disorders (ICHD-3) categorized secondary headache disorders into headaches attributed to head and/or neck trauma, cranial and/or cervical vascular disorder, nonvascular intracranial disorder, substance abuse or withdrawal, infection, disorders of homeostasis, disorders of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cervical structures and, finally, headache attributed to psychiatric disorders.⁸

Brain imaging is essential to rule out a serious secondary headache disorder. In a previous study from the U.S, 4% of patients who presented to the ED with a headache had an intracranial pathology.⁹ Another study reported that 5.5% of headache patients who underwent head computed tomography (CT) scan in the ED were ultimately diagnosed with a pathological process.⁶ However, the financial burden of imaging is high.¹⁰ The American College of Radiology (ACR) appropriateness criteria have been developed to assist physicians in choosing the most appropriate imaging for headache disorders based on the clinical scenarios.¹¹ However, a recent study reported that a quarter of patients with chronic headache had a head CT performed upon visits to the ED, indicating a continued overuse of neuroimaging instead of relying on evidence-based criteria.¹²

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Generally, there is paucity of literature on the prevalence and types of secondary headaches presenting to EDs at tertiary hospitals in the Middle East. This study sought to determine the most commonly-reported diagnoses in patients who presented to the ED of a tertiary hospital and had neuroimaging for headache symptoms, either isolated or in combination with other neurological symptoms. Further, we explored the association between clinical features and abnormal neuroimaging.

Methods. Literature review. Search through Midline and PubMed libraries was made using relevant terminology including “headache and neuroimaging”, “headache in the emergency department” and “headache in Saudi Arabia emergency department” and others were used, all relevant articles were reviewed, and references of subsequent articles were reviewed as well.

Participants and institution. This retrospective chart review study was conducted at King Saud University Medical City (KSUMC), Riyadh, Saudi Arabia. The KSUMC is a tertiary academic center located in the capital and largest city in Saudi Arabia. The ED of KSUMC receives walk-in patients as well as ambulance-transferred cases from different primary, secondary and tertiary specialized care centers located mainly within the Riyadh region, but also from other regions of Saudi Arabia. Patients arriving at the KSUMC ED with a headache symptom are managed by either an emergency physician and/or neurology consultation team, and many of those patients eventually undergo

Table 1 - Patients' characteristics at the time of presentation.

Variables	n (%)
Women	219 (66.6)
Age, mean (SD) years	39.7 (18.4)
Post-partum	10 (3.0)
Pregnancy	12 (3.6)
Oral Contraceptive use	13 (4.0)
Known migraineurs	28 (8.5)
Previous neurological disease	48 (14.6)
Previous stroke	16 (4.9)
Seizures	10 (3.0)
Known idiopathic intracranial hypertension	7 (2.1)
Other	16 (4.9)
Hypertension	73 (22.2)
Diabetes Mellitus	63 (19.1)
Connective tissue disease	34 (10.3)
Known hypercoagulable state	4 (1.2)

Data are number (%) unless otherwise noted

Table 2 - Headache characteristics and neurological examination findings.

Variables	n (%)
Onset after age of 50 years	66 (20.1)
Headache severity	
Mild to moderate	23 (7.0)
Severe	120 (36.5)
Missing	186 (56.5)
Headache character	
Throbbing	82 (24.9)
Compressing	40 (12.2)
Dull or achy	8 (2.4)
Stabbing	5 (1.5)
Missing	194 (59.0)
Headache location	
Temporo-parietal	63 (19.1)
Holo-cephalic	46 (14.0)
Occipital	37 (11.2)
Bitemporal	30 (9.1)
Frontal	20 (6.1)
Retro-orbital	8 (2.4)
Missing	125 (38.0)
Headache onset	
<1 week	102 (31.0)
1 week to 1 month	45 (13.7)
>1 month	51 (15.5)
Missing	131 (39.8)
Headache duration >4 hours	26 (7.9)
Neck pain	49 (14.9)
Neurological signs	144 (43.8)
Papilledema	35 (10.6)
Sensory abnormality	24 (7.3)
Weakness	23 (7.0)
Seizure	13 (4.0)
Cranial nerve palsy	14 (4.3)
Visual disturbance	11 (3.3)
Dysarthria or aphasia	7 (2.1)
Other	17 (5.2)

Data are number (%) unless otherwise noted

neuroimaging. All neuroimaging studies at our center are read by a neuroradiology specialist. We reviewed the electronic neuroradiology database between June 1, 2015 and May 31, 2019 to identify eligible patients. The medical records of eligible patients were also reviewed. We included all patients who presented to the ED with headache, either as an isolated symptom or in combination with other neurological symptoms, and patients who had neuroimaging with either a head CT and/or magnetic resonance imaging (MRI). All neuroimaging requests that had 'headache' listed among the indications for imaging were included.

Table 3 - Imaging modality and diagnoses (n=329).

Variables	n (%)
Neuroimaging performed	
CT head	262 (79.6)
MRI brain	255 (77.5)
Both CT and MRI	188 (57.1)
Abnormal neuroimaging	105 (31.9)
Final diagnosis as reported	
Primary headache	54 (16.4)
Migraine	47 (14.3)
Tension-type	5 (1.5)
Cluster	1 (0.3)
Hemicrania continua	1 (0.3)
Secondary headache	160 (48.6)
Idiopathic intracranial hypertension	33 (10.0)
Ischemic stroke	21 (6.4)
Brain tumor	19 (5.8)
Intracranial hemorrhage	13 (4.0)
CNS infection	12 (3.6)
Cerebral venous thrombosis	10 (3.0)
Other	52 (15.8)
Non-specific headache	115 (35.0)

Data are number (%) unless otherwise noted

Neuroimaging requests received from the outpatient clinics or for electively-admitted patients were excluded. The study was approved by the local institutional review board. Given the retrospective design of the study, informed consent was waived. The study is in agreement with the Declaration of Helsinki principles.

Study variables. Data collected were demographics, headache characteristics, previous neurological or medical disorders, neurological examination findings, neuroimaging results, and the reported headache diagnosis. We characterized headache disorders based on the documented final diagnosis upon discharge into primary headache disorders, secondary headache disorders, or non-specific headaches when no clear diagnosis was documented. Neuroimaging was categorized based on the reported diagnosis by the neuroradiologist into normal or abnormal. Neuroimaging reported with non-specific findings, such as a few small white matter T2/Flair hyperintensities, were further reviewed by a neurologist (M.A.) to determine their significance in relation to the clinical diagnosis.

Analysis. Continuous variables were presented as mean and standard deviation (SD). Categorical variables were presented as counts and frequencies. A Chi-square test was used to assess for associations between the

dependent variable (neuroimaging: normal vs abnormal) and the independent variables including age (≤ 50 vs > 50 years), gender, headache onset (≤ 1 month vs > 1 month), headache features, abnormal neurological signs, history of a previous neurological disease, history of connective tissue disease, hypercoagulable state, oral contraceptive use, and headache onset during pregnancy or post-partum. The variables that showed significant associations with the dependent variable were entered into a logistic regression model. Odd ratios (ORs) and 95% Confidence Intervals (CIs) were computed for each independent variable. No imputation was carried out for missing data. A two-tailed p -value of <0.05 was considered significant. The statistical analysis was performed using SPSS Statistics for Macintosh, version 25 (IBM, Armonk, NY).

Results. We included 329 patients (33.4% men, 66.6% women) who had headaches among their presenting symptoms to the ED and who underwent neuroimaging. The mean age (SD) was 39.7 (18.4) years. Among all participants, 8.5% of the patients reported having been diagnosed with a migraine headache at the time of ED presentation, and 14.6% had been previously diagnosed with a neurological disease (Table 1). Headache characteristics and neurological examination findings are shown in Table 2. Approximately 43.8% of the patients had at least one neurological sign upon presentation (Table 2). Approximately half of the patients were diagnosed with a secondary headache disorder (Table 3). The most common secondary headache disorder was idiopathic intracranial hypertension (IIH), which constituted approximately 10% of all patients, followed by ischemic stroke (6.4%) and brain tumor (5.8%). Approximately one-third of the patients had a non-specific headache. The remainder (16.4%) had a primary headache disorder, the most common being migraines. All patients had neuroimaging, and 31.9% had abnormal results that explained their clinical presentation of a secondary headache disorder (Table 3).

In the bivariate analysis, the independent variables that showed significant associations with abnormal neuroimaging were headache onset ≤ 1 month (OR 3.22, CI 1.46 – 7.10, $p=0.003$), age of onset >50 years (OR 2.02, 95% CI 1.16 – 3.52, $p=0.012$), and presence of an abnormal neurological sign (OR 4.54, 95% CI 2.70 – 7.62, $p<0.001$). However, with further analysis using a multivariate logistic regression model (194 cases included), patients who had an abnormal neurological sign (OR 3.60, CI 1.89 – 6.83, $p<0.001$), and those with headache onset ≤ 1 month (OR 3.37, CI

1.47 – 7.70, $p=0.004$) had a significantly higher OR of abnormal neuroimaging.

Discussion. This study reports the most common diagnoses in patients who had neuroimaging in the ED of a tertiary hospital for a headache disorder. The study revealed that the majority of the patients had either a secondary headache or non-specific headache disorder, and only a sixth had a primary headache disorder.

This finding is explained by the study inclusion criteria limited to patients that had neuroimaging, which would ideally be requested when a worrisome diagnosis is clinically suspected. Although headache is a common symptom in the ED,^{6,9} and most cases are due to a primary headache disorder or benign etiologies,^{6,13,14} it remains essential to risk-stratify those patients for the need for radiological and advanced laboratory investigations.

Generally, a non-enhanced head CT is one of the most preferred modalities of neuroimaging in the ED.¹⁵ It has been reported that approximately 14% of patients with headache in the ED have undergone neuroimaging, 95% via CT with a diagnostic yield of 5.5%.⁶ Approximately a third of our sample had abnormal neuroimaging that influenced the diagnosis, and all were diagnosed with secondary headache disorder. Ischemic strokes accounted for 6.4% of the final diagnoses, intracranial hemorrhage 4%, and CNS infection 3.6%, whereas the corresponding proportions reported in another study from the U.S were 0.8%, 0.6%, and 0.5%, respectively.⁶ This discrepancy is likely because of a difference in the study population where the latter study included all headache patients presented to the ED whether or not they had neuroimaging.⁶

In addition, we attempted to identify headache characteristics that increased the yield of neuroimaging in the emergency setting. In our cohort, the presence of abnormal findings upon neurological examination was significantly associated with abnormal neuroimaging. This finding has also been observed in other studies.⁹ The American Family Physician guidelines for imaging in nonacute headache indicates that the presence of abnormal findings on neurological examination has a likelihood ratio of 3.0 (95% CI 2.3 – 4) of finding a significant abnormality on neuroimaging, whereas a normal neurological examination reduces the likelihood ratio to 0.7 (95% CI 0.52 – 0.93).¹⁶ However, a normal neurological examination does not waive the need for neuroimaging in selected cases. Patients with serious neurological disorders such as cerebral venous thrombosis, reversible cerebral vasoconstriction syndrome, ischemic stroke, brain aneurysms, and meningitis may present with headache and have normal

neurological examination on first assessment.^{17–21} In such cases, the presence of other “red flags” should alert the physician to the necessity of neuroimaging; among those, headache related to activity or position, thunderclap headache, onset during pregnancy, head trauma, immunocompromised state, or cancer.¹¹ The timing of onset is another important clue to a possible secondary headache disorder; our data showed that a headache onset of less than 1 month is associated with a higher OR for an abnormal neuroimaging. This is in line with previous reports of the association between recent-onset headache and abnormal neuroimaging.¹⁶ Furthermore, headache prevalence decreases with age;¹ therefore, onset at age 50 or older is recognized as a “red flag” for a secondary headache disorder, and has been reported to have significant associations with CNS pathologies.^{6,9}

It is important to emphasize that fundoscopy should be performed in all patients presenting with headache. Optic disc edema may be the only neurological sign indicating a secondary headache disorder. In such cases, the American College of Radiology (ACR) recommends an MRI on the brain (with and without contrast) for patients presenting with headache and papilledema.¹¹ The incidence of IIH in the Middle East countries has been estimated to be higher than that in the Western countries.²² A recent study conducted in Kuwait revealed a crude annual incidence of IIH of 3.28 per 100,000 of the general population, wherein 60% of them had a BMI >30.²³ Similar to the Western countries, obesity has been reported as a risk factor for IIH in the Middle East countries including Saudi Arabia.^{22–24} A striking finding in this study is the relatively high proportion of IIH (10%) among our patients. This is likely explained by the fact that our studied ED receives direct referrals from the affiliated Ophthalmology centers in the city. Those referrals are typically made to facilitate urgent neurology assessment and obtain neuroimaging, and mostly include patients with optic disc edema. Therefore, the logistics of such referrals to our ED rather than to the outpatient neurology clinic have probably introduced bias in our sample.

Finally, the ACR discourages the use of neuroimaging for classic migraine, tension-type headache, or chronic headache unless a new feature or neurologic deficit is present.¹¹ Nonetheless, a considerable portion of our patients who had undergone neuroimaging had a primary headache disorder, mostly migraines, or non-specific headaches. This suggests a possible overuse of neuroimaging in the ED, and urges adoption of evidence-based criteria such as those published by the ACR.¹¹

Limitations. The retrospective design of our study has all the inherent limitations of such studies. Missing data and inconsistencies in documentation of headache characteristics and neurological examination findings are possible sources of bias. Another limitation is the likely presence of referral bias explaining the relatively high prevalence of IIH and possibly other positive imaging findings. Furthermore, the fact that we studied visits from the ED will exaggerate the referral bias as a referral through ED is the preferred route for urgent cases in our region, compared to a referral to urgent outpatient clinics in developed countries. The diagnostic uncertainty and large percentage of headaches labeled as non-specific is another major limitation. Factors that play a role in this have previously been explored by Granto et al²⁵ who surveyed emergency physicians and concluded that the majority (96%) did not know the ICHD-3 criteria. It appears that the percentage in our study of headaches that were labeled as “non-specific” is similar compared to other studies.^{25–27}

Implications of this study for future practice include the need for further studies about the frequency and types of secondary headaches in Saudi Arabia; particularly to explore the incidence and prevalence of disorders that were surprisingly common in our data such as IIH. Other implication would be to study the economic burden of over investigation headaches especially in the context of government financed healthcare.

Conclusion. Among patients who presented to the ED of a tertiary hospital with a headache and who subsequently had neuroimaging performed on them, a secondary headache disorder was diagnosed in approximately a half, and the most common secondary headache disorder was IIH. Among all the study patients, neuroimaging abnormalities were reported in approximately a third of all subjects and were associated with the presence of abnormal neurological signs and a headache onset of ≤ 1 month. Further studies are required to investigate the potential overuse of neuroimaging, and to assess the use of risk-stratification criteria for headache patients in the ED.

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