

**Research Article**

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## Unraveling the enigma: Unveiling transient global amnesia- debunking risk factors and investigative conundrums

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**Abstract****Introduction:** Transient Global Amnesia (TGA) is a neurological condition characterized by a temporary dysfunction of the episodic memory system.**Objectives:** In this short communication, we present the clinical and paraclinical features of TGA cases collected at the neurology emergency unit. Through a literature review, we explore the potential role of preexisting risk factors in increasing the risk of TGA.**Patients and methods:** This prospective study covers the period between January 2020 and December 2020, during which we collected data from 12 patients at the neurology emergency unit of the University Hospital of Marrakech, Morocco. All patients met the Hodges-Warlow criteria for TGA.**Results:** The sample consisted of 6 men and 6 women with an average age of 57 years. The duration of TGA episodes in our series ranged from 30 minutes to 24 hours, during which all patients experienced an acute failure of episodic memory. Among the cases, 5 patients had preexisting risk factors, including migraine, amphetamines intoxication, and unusual physical effort. Neurological assessments revealed no focal motor, speech, sensory, coordination, or cranial nerve deficits. Brain magnetic resonance imaging showed no acute abnormalities in 11 patients, while one case exhibited punctiform hypersignal at the lateral part of the hippocampus.**Conclusion:** The incidence of TGA is often underestimated due to the absence of physical signs, the ability of patients to continue their activities, the brief duration of symptoms, and the recovery without long-term effects. The etiology of TGA remains unknown, but it is believed to be a multifactorial disorder with certain triggering factors.**Keywords:** Amnesia; Anterograde amnesia; Transient global amnesia; Triggering factors.

## Introduction

Transient Global Amnesia (TGA) is a neurological condition characterized by a temporary dysfunction of the episodic memory system, which spontaneously and completely resolves in less than 24 hours [1,2]. The pathophysiological mechanisms underlying TGA are still uncertain [2,3], and the incidence of TGA is often underestimated [4].

This syndrome is defined according to Hodges and Warlow's criteria, which include anterograde amnesia witnessed by an observer, absence of clouding of consciousness or loss of personal identity, cognitive impairment limited to amnesia, absence of focal neurological or epileptic features, no recent history of head trauma or seizures, and resolution of symptoms within 24 hours [5]. TGA is diagnosed based on clinical presentation, and confirmation can be obtained through diffusion sequence MRI, which shows punctuate hyperintense signals in the CA1 field of the hippocampus. The hippocampus is a crucial structure for episodic memory [3]. The prognosis for TGA is generally favorable [2,6].

The specific objective of our study is to describe the clinical and paraclinical features of TGA cases collected at the neurological emergency unit, and to explore whether preexisting risk factors contribute to an increased risk of TGA through a literature review.

## Patients and methods

This prospective observational study was conducted in the Marrakech region from January 1, 2020, to January 1, 2021, with a primary focus on patients diagnosed with amnesic ictus. The study's inclusion criteria were based on Hodges' criteria, which were established by Hodges and Warlow in 1990. These criteria were employed to identify and select patients who fulfilled the specific requirements for an amnesic ictus diagnosis.

To acquire pertinent information, data were collected from the medical records of the enrolled patients. The medical records served as the primary source of comprehensive details concerning the patients' medical histories, diagnostic procedures, and any other relevant information that could contribute to the study's objectives.

Our study utilized a questionnaire that was completed based on the patients' medical records. The questionnaire consisted of two parts.

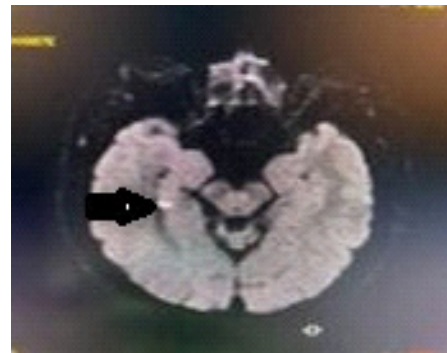
The first part of the questionnaire focused on gathering demographic information, such as age and sex, as well as socioeconomic characteristics. The second part of the questionnaire encompassed various aspects, including positive diagnosis, risk factors, past medical history (such as hypertension, diabetes, hyperlipidemia, atrial fibrillation, stroke, migraine, and transient global amnesia attacks), trigger factors, and details regarding diagnostic imaging methods such as Computed Tomography (CT) scans and Magnetic Resonance Imaging (MRI).

The data obtained were subsequently analyzed using Microsoft Excel for Windows version 2007. Statistical analyses were performed to derive meaningful insights and draw conclusions from the collected data.

## Results

The average age of our patients was 57 years, ranging from 22 to 79 years. Among the patients, 50% were male and 50% were female. Forty percent of the patients had a medical history that included epilepsy, migraine, hypertension, smoking, dyslipidemia, atrial fibrillation, and migraine. Only one patient had a history of three episodes of amnesic ictus. Among the 12 cases of amnesic ictus in our series, five patients had triggering factors, including migraine, amphetamines, cold baths, and unusual physical effort.

The onset of Transient Global Amnesia (TGA) occurred in the summer for five cases, in winter for three cases, and in spring for four cases. The average duration of the amnesic episode was 6 hours and 30 minutes. The symptomatology presented abruptly in all patients, characterized by anterograde amnesia. Neurological examination results were normal for all patients. They exhibited proper orientation in time and space, and their long-term memory was intact.



**Figure 1:** MRI brain, axial section, showing a punctiform hypersignal at the lateral part of the hippocampus (arrow).

Regarding the paraclinical examination, laboratory tests, including complete blood count, thyroid function tests, glycemia, blood electrolytes, and infectious tests, were within normal ranges. Electrocardiograms showed normal sinus rhythm for all patients. Brain Magnetic Resonance Imaging (MRI) revealed no acute abnormalities in 11 patients, while one case showed a punctiform hypersignal at the lateral part of the hippocampus (Figure 1).

The medical records of the patients are succinctly summarized in Table 1.

## Discussion

Transient Global Amnesia (TGA) is an acute benign reversible neurological state characterized by episodic memory dysfunction. The incidence of TGA is likely underestimated [4]. Among individuals aged 50 years or older, the estimated incidence is 23.5 to 32 per 100,000 per year [4]. This underestimation may be attributed to the absence of physical signs, the ability to continue with current activities, the short duration of symptoms, and the absence of long-term consequences. The male-to-female ratio is balanced [7]. TGA primarily affects the elderly [6], with an average age of onset for the first episode around 60 years [7]. The duration of TGA episodes typically lasts between 1 hour and 24 hours [6]. A triggering factor is identified in over 50% of cases [8].

**Table 1:** Demographic, clinical and neuroimaging features of patients with TGA.

Patients	Age	Gender	Medical history	History of TGA	Triggering factors	Season	Duration of TGA	Neurological exam	MRI
1	54 years old	Female	Epilepsy	No	No	Winter	24 hours	Normal	Normal
2	60 years old	Male	Migraine	No	Migraine	Summer	2 hours	Normal	Not done
3	22 years old	Male	No	No	Taking amphetamine	Winter	5 hours	Normal	Normal
4	79 years old	Male	-BPH for 14 years -Prostate adenoma - Left sural phlébitis	3 épisodes of TGA	No	Summer	3 hours	Normal	-Small ischemic sequelae deficiency in the right caudate nucleus and the left lenticular nucleus.
5	52 years old	Male	-Smoking -Dyslipidemia -family pathological antecedents: Stroke	No	No	Spring	4 hours	Normal	-Leucoencephalopathy -Leukoaraiosis
6	50 years old	Male	No	No	Cold baths	Spring	30 minutes	Normal	Normal
7	63 years old	Female	No	No	Unusual physical effort	Spring	1 hour	Normal	Normal
8	64 years old	Female	No	No	Unusual physical effort	Summer	24 hours	Normal	Normal
9	51 years old	Female	No	No	No	Summer	5 hours	Normal	Normal
10	33 years old	Female	No	No	No	Summer	1 hour	Normal	Normal
11	73 years old	Male	Atrial fibrillation for 5 years	No	No	Spring	5 hours	normal	Punctiform hypersignal at the lateral part of the hippocampus.
12	60 years old	Female	No	No	No	winter	2 hours	normal	Normal

The most commonly reported triggering factors for TGA include intense emotion, acute pain, unusual physical effort, cold baths, sexual relations, alcohol consumption, severe nightmares, and high altitude [7]. Some authors suggest the involvement of precipitating psychological factors. Migraine has a strong association with TGA, as reported by Sander and Miller [9]. The recurrence rates of TGA range from 2.5% to over 5% [7].

The occurrence of TGA is higher in the spring and summer seasons [10], with a predominance in the morning [11]. In our series, there were 5 cases of amnesic ictus occurring in the summer, 3 cases in winter, and 4 cases in spring.

The diagnosis of TGA is based on the diagnostic criteria established by Hodges and Warlow and can be confirmed through diffusion sequence MRI [3,5].

Emergency MRI is typically recommended for individuals under 50 years of age and in the presence of vascular risk factors [3].

Brain MRI commonly shows a localized restriction of the diffusion coefficient in the mesio-temporal region within 48 to 72 hours after the onset of the amnesic episode [1,3].

Perfusion MRI reveals a decrease in cerebral blood flow and volume in both the hippocampus and subcortical structures belonging to the Papez circuit [12]. However, in some cases, MRI

results may appear normal [1].

The exact pathophysiology of TGA remains unknown, but hypotheses include arterial and venous dysfunction, migraines, epilepsy, and psychogenic disorders. Recent research suggests that the vulnerability of CA1 neurons to metabolic stress plays a central role in the pathophysiological cascade, leading to impairment of hippocampal function during TGA [13].

Two pathophysiological mechanisms have been proposed to explain the connection between migraine and transient global amnesia. The first hypothesis suggests an invasive cortical depression that passes through the hippocampal cortex, acting as a trigger responsible for vasoconstriction and transient metabolic stress, leading to hippocampal dysfunction [14]. The second hypothesis suggests an increase in intracranial venous pressure. Migraine patients have been found to have a defect in venous vasodilation and increased venous flow into the inner jugular vein during migraine attacks, potentially increasing the risk of venous congestion after a Valsalva strain [15].

Migraine is associated with an increased risk of TGA [13,16]. There is no significant difference between migraines with and without aura. The risk is particularly higher for women aged 40-60 [10]. However, there is currently no evidence to suggest that transient global amnesia may serve as an aura for a migraine attack. On the contrary, a recent study indicates that the head-

ache precedes the amnesia and not the other way around [17].

Several studies have shown that individuals with transient global amnesia do not have a higher prevalence of cardiovascular risk factors compared to the general population [18,19].

The hypothesis of an epileptic mechanism causing amnesic episodes is no longer accepted [3]. No studies have demonstrated the presence of epileptic abnormalities during the acute phase or after the episode. Patients with transient global amnesia are not at risk of subsequent epileptic seizures [3].

Transient global amnesia can be considered a complex epileptic phenomenon, and the cumulative effect of various triggers may contribute to the recurrence of this unique event in an individual's life [20].

### What to believe?

It's important to understand that TGA is a diagnosis of exclusion. This means that once other potential causes of memory loss have been ruled out through investigations, and the symptoms align with the typical characteristics of TGA, the diagnosis may be made.

While pre-existing risk factors can provide some insight into the likelihood of experiencing TGA, they are not definitive predictors, nor are they causative factors. TGA can occur in individuals without any known risk factors, and having risk factors does not guarantee that an episode of TGA will occur.

The experience gained from treating these patients has not only depend our understanding of amnesic stroke but also highlighted the importance of prompt diagnosis and specialized care.

Hospital Mohammed VI Marrakech continues to strive for excellence in patient care and remains committed to unraveling the mysteries of amnesic stroke, and fostering a brighter future for all those affected.

**Limitations:** In our study, memory scales were not utilized to assess memory in TGA patients. However, recent studies have indicated that even after the resolution of TGA symptoms, patients may still exhibit abnormal memory behavior. Therefore, it is recommended that future research incorporate memory scales to quantitatively evaluate whether TGA patients experience memory sequelae and gain further insights into this matter.

### Conclusion

Transient Global Amnesia (TGA) is characterized by a temporary and reversible global amnesia that spontaneously resolves within 24 hours. The diagnosis of TGA relies on clinical findings and can be further confirmed through the use of MRI. While the exact pathophysiology of TGA remains unclear, there is evidence suggesting that risk factors play a role in its occurrence. However, further research is needed to fully understand the underlying mechanisms and clarify the pathophysiology of this clinical syndrome.

To advance our understanding of TGA, more studies are necessary to explore its underlying mechanisms and etiology. Investigating potential risk factors and their influence on TGA occurrence can provide valuable insights into preventative strategies or early interventions. Additionally, research focused on the pathophysiological processes involved in TGA can shed light on the neurological basis of this transient condition.

### What is known about this topic?

Diagnostic criteria for TGA are based on clinical presentation and can be confirmed through imaging techniques such as diffusion sequence MRI.

### What this study adds?

This study conducted at Mohammed VI Hospital provides valuable insights into the assessment and follow-up of TGA patients. In this particular study, memory scales were not employed to evaluate the memory of TGA patients. However, the study emphasizes the importance of utilizing memory scales in future research endeavors to quantitatively assess whether TGA patients experience persistent memory sequelae. This approach may contribute to a more comprehensive understanding of the long-term effects of TGA and provide thorough information regarding the state of patients' memory after the resolution of TGA symptoms. By highlighting the significance of incorporating memory scales in the assessment of TGA patients, this study suggests a potential direction for further research to advance our knowledge of this intriguing neurological condition.

### Declarations

**Conflicts of interest:** The authors have no potential conflicts of interest to disclose.

**Authors' contributions:** All the authors have read and agreed to the final manuscript.

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