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Seasonal variations in the occurrence of transient global amnesia (TGA)

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Abstract

Background. Transient global amnesia (TGA) is a rare, benign condition characterised by a sudden deficit of anterograde and retrograde memory that usually lasts for a few hours and is not accompanied by other focal neurological symptoms or signs. Its aetiology is still unclear. Various events or activities may trigger TGA. Evidence of seasonal variations in the appearance of TGA is inconsistent.

Methods. We retrospectively analysed the medical history of 114 adult patients with diagnosed TGA, hospitalised at two neurology departments in Wrocław from 2008 to 2014. We reviewed risk factors, trigger points, and occurrence in each month of the year in our patient population.

Results. Over this seven-year period, 114 patients were diagnosed with TGA. The annual occurrence ranged from 13 to 22 hospitalisations. The mean age of the patients was 64 years. There were 36 TGA events in men and 78 in women. TGA occurred most frequently in spring (36%) and summer (30%), with the incidence peaking during March.

Conclusions. Our findings suggest that there is a relationship between the season of the year and the probability of TGA.

Key words: transient global amnesia, seasonal variations
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Introduction

Transient global amnesia (TGA) is a rare condition characterised by a sudden deficit of anterograde and retrograde memory that lasts up to 24 hours. The episodes are sudden, transient, benign and not accompanied by other neurological symptoms [1]. The incidence varies between 3 and 8 cases per 100,000 people per year; the majority of cases occur in people aged between 50 and 70 years and only rarely in patients younger than 40 [2]. The rate of recurrent attacks within one year varies between 6% and 10% [3]. The aetiology and pathomechanism of TGA are not clearly defined. Transient ischaemic attack (TIA), venous congestion with subsequent ischaemia, epilepsy, and migraine have been suggested as possible causes [3–5]. Magnetic resonance imaging (MRI) studies indicate that CA1 neurons of the hippocampal area play a role in the pathomechanism of TGA [6–9]. These areas are sensitive to metabolic stress, oxidative stress, and cytotoxic glutamate. One in three patients experiences a preceding event immediately before a TGA episode, especially emotional stress, physical activity, acute pain, or immersion in cold water [3]. Atmospheric factors such as air pollution, UV radiation, temperature, and air pressure also play an important role in the pathogenesis of TGA.

The aim of this study was to evaluate the seasonality of TGA and the possible influence of the seasons on the incidence of TGA.

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Table 1. Criteria of TGA according to Hodge and Warlow [2]

Sudden anterograde and retrograde amnesia in the presence of witnesses of the event
No disturbance of consciousness; awareness of personal identity is preserved
Cognitive impairment limited to amnesia
No focal neurological signs
Exclusion of head or neck injury, or other causes of amnesia; lack of epilepsy in medical history
Attack resolves within 24 hours

Table 2. Demographic data of patients

Time of observation: 2008–2014				
n = 114, mean age 64.32 ± 10.52 years				
F: n = 78, mean age 65.36 ± 10.29 years				
M: n = 36; mean age 62.06 ± 10.80 years				
Risk factors				
Hyperten-sion	Diabetes	Ischaemic disease	Thyroid dysfunction	Hyper-lipidemia
61 / 114	5 / 114	13 / 114	15 / 114	30 / 114

Material and methods

We retrospectively analysed the medical history of 114 adult patients with diagnosed TGA, hospitalised at two departments of neurology in Wrocław between 1 January 2008 and 31 December 2014. TGA was diagnosed according to the criteria created by Hodge and Warlow in 1990 (Tab. 1) [10]. All participants in the study underwent a neurological examination, brain CT scan without contrast, laboratory tests, EEG, and Doppler scanning of vessels. We excluded patients with transient ischaemic attack (TIA) and stroke.

In addition, in 2016 patients who had experienced a TGA in the previous one to seven years were sent a questionnaire asking about their vascular diseases and past TGA incidents.

Ethical approval and patient consent were not required.

All analyses were performed using Statistica 10 software. Pearson's chi-square test was used for categorical variables. The threshold of statistical significance was $\alpha = 0.05$.

Results

TGA was diagnosed in 114 patients (78 women, 36 men) with a mean age of 64.3 ± 10.52 years (range 27–87) and with a median of 63.0. In our group, the annual occurrence of TGA ranged from 13 to 22 hospitalisations. Table 2 shows the demographics, basic clinical data, and risk factors. Loss of memory lasted between 30 minutes and 13 hours. A precipitating event was noted in 37 cases (65.6%). In 21 patients, an increase of blood pressure may have been the triggering factor. In other cases, the attacks were precipitated by stressors such as physical activity, medical appointment, insect bite, trauma, exposure to the sun, sauna, gastroscopy, headache, and nutritional factors.

According to the modified Rankin scale, all patients had a score of 0. In 63.1% of the cases (72 patients) the neurological examination was normal. The remaining patients had some abnormalities. The most common abnormality was weakened ankle jerk reflex. Nineteen patients who had suffered TGA in the summer had an abnormal neurological state, in most cases asymmetrical deep tendon reflexes without paresis. Non-contrast head CT performed on admission was normal in 46.5% of the patients. The remaining 53.5% of patients had changes in the white matter characteristic of cerebral small vessels disease.

Figures 1 and 2 show, respectively, the incidence of TGA in each month and season. The highest incidence was during the spring and summer months, with the peak incidence occurring during March (17 patients) and the lowest rate in September (five patients) (Tab. 3). Seasonal peaks in the incidence of TGA were noted in spring and summer (Tab. 4).

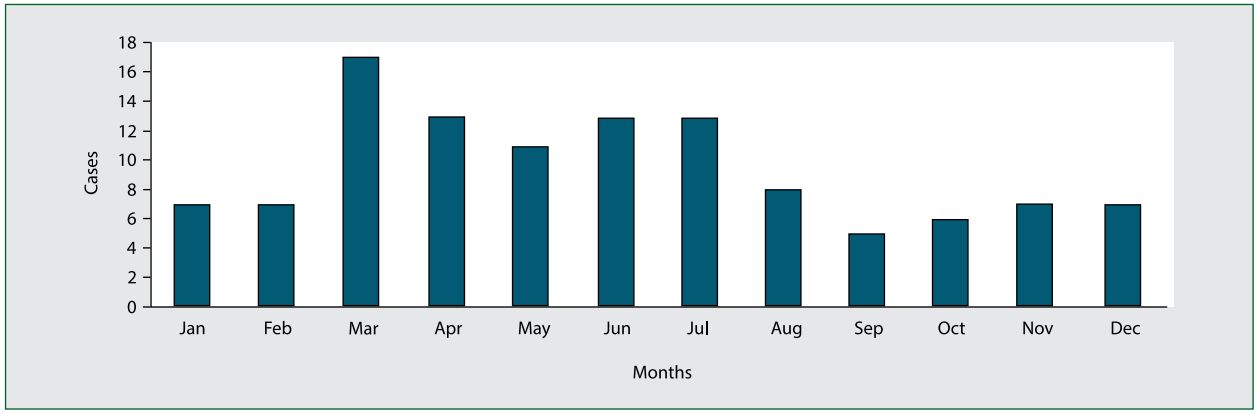

Figure 1. Incidence of TGA per month

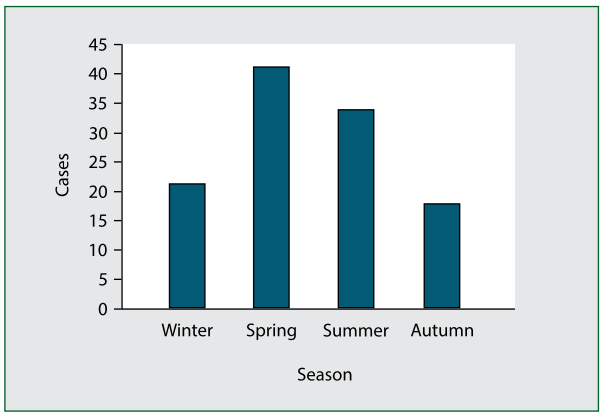

Figure 2. Incidence of TGA per season

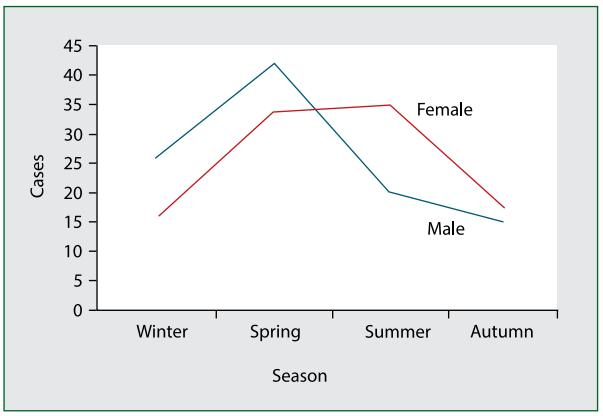

Figure 3. Incidence of TGA per gender (F/M) and season

Table 3. Percentage of TGA incidence according to season

Season	Mean	Convidence interval	Median	STD
Winter	17.4	9.5–25.4	21	8.6
Spring	34.4	21.4–47.5	30	14.1
Summer	30.9	18.5–43.4	35	13.4
Autumn	17.2	7.5–26.9	17	10.5

Table 4. Percentage of TGA incidence according to month

	Mean	Convidence interval	Median	STD
Jan	6.4	1.4–11.3	7.1	5.4
Feb	5.0	0–11.6	0.0	7.1
Mar	14.3	3.8–24.8	11.1	11.4
Apr	10.3	3.1–17.4	14.3	7.7
May	9.9	6.5–13.3	9.1	3.7
Jun	13.1	3.2–23.1	14.3	10.7
Jul	10.5	0–22.9	0.0	13.4
Aug	7.3	2.7–11.8	7.1	4.9
Sep	5.0	1.8–8.3	7.1	3.5
Oct	5.7	1.1–10.3	5.6	5.0
Nov	6.5	2.2–10.8	5.6	4.7
Dec	6.0	0–12.6	7.1	7.2

The Chi-square test indicates the largest incidence in the spring and summer months ($p = 0.013$). There was a predominance of women in all months of the year except for May and December. Among women, the largest (30%) incidence of TGA was in summer and in spring; among men more than 40% of incidence took place in spring (Fig. 3).

Based on the 37 questionnaire results, recurrent TGA occurred in three cases, one person had ischaemic stroke, and one case occurred with transient ischaemic attack.

Discussion

TGA is a neurological disorder with an unknown and complex pathogenesis. Its mechanisms are still unclear, including vascular aetiology, seizure and migraine. The presence of focal-high-signals abnormalities in the hippocampus on diffusion-weighted imaging (DWI) is very suggestive of TGA [11, 12]. The frequency of DWI signal abnormalities in patients with TGA varies widely, from 0% to 84% [13]. Also, silent small lacunar infarcts are detectable on conventional MRI [14, 15].

Its seasonal appearance, with a peak in March (which was confirmed in our retrospective study), may imply an atmospheric influence. In a six-year study involving a group of 223 patients in northern Italy, Akkawi et al found the peak incidence to be in the autumn–winter period, which indicates a correlation with low temperatures [16]. By contrast, the authors of an Israeli study observed an increase in TGA incidence in the winter-spring months, peaking in December and March [17]. These differences may result from different geographical locations or the coexistence of other atmospheric factors. We know from electrophysiological and biochemical studies that several functions of the nervous system change periodically. It has also been confirmed that the morbidity of several diseases is dependent on meteorological and climatological factors. The meteorological factors activate the autonomic nervous system, which may lead to certain diseases or exacerbate some symptoms by affecting the homeostasis. The climatological factors that are present in a given geographical region may stimulate a disease or weaken the human organism. In epidemiological studies, it has been shown that as much as 90% of strokes are correlated with the movement of weather fronts [18]. Seasonal diseases include depression (peaking in autumn-winter), epilepsy, and vascular brain disorders. Migraine is dependent on daily as well as annual cycles (with the peak in January) and atmospheric factors (for example, local winds). Multiple sclerosis patients have symptoms that change throughout the day. This disease is also known to spread differently in different geographic locations. Vascular

brain diseases are dependent on meteorological factors, such as air temperature and pressure [19, 20]. Haemorrhagic and subarachnoid strokes are also seasonal diseases, with peak incidence in autumn and winter [21].

In our TGA patient group, there were significantly more women than men (similar to other studies e.g. Melo et al. 1992, Lauria et al. 1997, and Keret et al. 2016) [17, 22, 23]. The relationship between patient gender and TGA is very unclear. Brigio et al. observed a higher incidence among men [24]. Other studies found no correlation. TGA-precipitating factors were observed only in 30% of the patients, and they were higher blood pressure and increased stress. In other studies, such factors were observed in 50–90% of the patients [6, 25]. Surveys have not shown an increased risk of recurrent TGA (similarly as with other vascular diseases).

In our study, the most frequent TGA comorbidity was hypertension, present in 54% of the patients. Epidemiological studies do not clarify which vascular disease risk factors are significant for TGA (unlike for stroke and TIA). Nevertheless, the following factors are thought to increase the likelihood of TGA: hypertension, diabetes, hypercholesterolemia, migraine, and psychological factors [3, 5]. In addition, Patoni mentions personality disorders, emotional instability and depressive anxiety, and a history of psychiatric disease in the family [26].

Our study confirmed the seasonal character of TGA, and the potential influence of geographic location and climate. The seasonality of TGA requires more clinical research in cooperation with weather stations in order to precisely determine the air pressure, humidity, and temperature fluctuations.

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