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# Cluster seizures and status epilepticus in new onset seizures among adult Egyptians



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## Abstract

**Background:** New onset seizure (NOS) is defined as the first seizure within a 24-h period ever experienced by the patient. Cluster seizures (CS) or status epilepticus (SE) can be the first manifestation of epilepsy or it may be a symptom of a brain tumor, a systemic disorder, an infection, or a syndrome. This study aims to determine the etiology of CS and SE in NOS among adult Egyptians. One hundred twenty adult Egyptian patients presented with NOS were enrolled in a hospital-based cross-sectional observational study within a time period of 6 months from March till September 2018. All patients were subjected to neurological examination including mini mental status examination, laboratory, neuroimaging, and electroencephalogram.

**Results:** Among 120 adult patients presented with NOS, males were prevalent (63%). Older adults (> 55 years) were prevalent (60%). Of the patients, 25% presented by CS, while 11% presented by SE. Post-stroke epilepsy (41%) was the predominant etiology of NOS. Cerebrovascular diseases (CVDs) were the prevalent etiology of SE in NOS (35%). NOS presented by CS were more prevalent among patients with brain tumors (29%) in comparison to CVDs (25%).

**Conclusion:** CS represented 25% of NOS in adult Egyptian patients. SE is prevalent among 11% of NOS. Despite CVDs being the most prevalent etiology of NOS in adult population (41%) including those presented with SE (35%), brain tumors are the most prevalent etiology of new onset CS (29%).

## Background

Seizure is defined as a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain [1].

Seizures are one of the important causes of morbidity and mortality in adults. Despite the many studies that are based on the seizure and epilepsy classification system, there are only a few studies on the clinical profile and causes of new onset seizures [2].

New onset seizure was defined as the first seizure (or the first cluster of seizures within a 24-h period) ever experienced by the patient [3].

A first ever seizure can be the first manifestation of epilepsy, which is characterized by recurrent unprovoked seizures (two or more). Or it may be a symptom of a

brain tumor, a systemic disorder, an infection, or a syndrome that deserves special attention and treatment [4].

Seizures are common in the general population and about 1 in 10 people will experience a seizure in their lifetime. Most of these seizures are provoked by acute events and are not related to epilepsy [5].

Epilepsy was regarded as a disease of children for many years, but as researchers gathered more data on an aging population, they found that the incidence of new onset epilepsy increased among people older than 50. They reported an incidence of 169/100,000 per year in this population, almost twice the incidence among children [6].

The incidence rate of new onset epilepsy in older adults ranges from 1 to 3 per 1000 person-years and is estimated to be two to six times higher than in younger adults [7].

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Etiology of seizures can be easily made out in most of the older patients. The causes include acute brain injury (subdural hematoma and stroke) and degenerative disorders (Alzheimer’s disease and malignancy). In most of the adult cases, a cause is most often autoimmune or paraneoplastic and infections (mostly viral encephalitis, although mycoplasma is not rare). They also can occur with systemic metabolic conditions like uremia, hyperglycemia, hypoglycemia, and hyponatremia. In the remaining, no cause is identified despite an extensive work-up. These cases are referred to as cryptogenic (NOS) or new onset refractory status epilepticus (NORSE) or NOS/NORSE of unknown etiology [8].

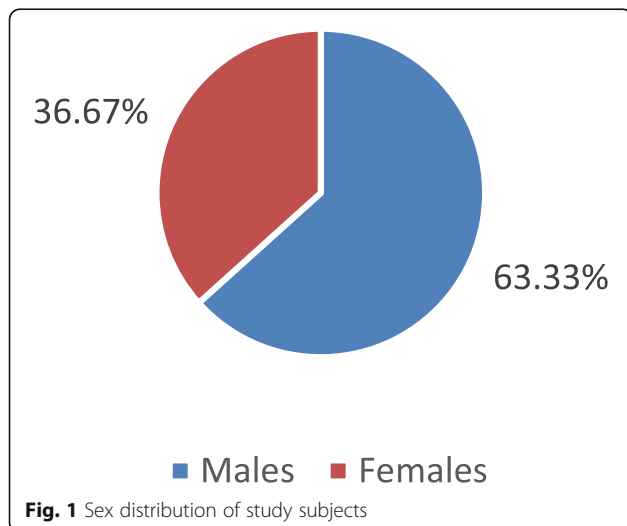
Acute repetitive seizures or cluster seizures are seizures of any type that may occur in groups or clusters over a number of hours or days. A person usually recovers between seizures and the clusters will end on their own [9].

Status epilepticus is a neurological emergency, which is defined as the occurrence of two or more convulsive seizures without full recovery of consciousness between the seizures or continuous convulsive activity lasting for more than 5 min and more than 10 min if non-convulsive [10].

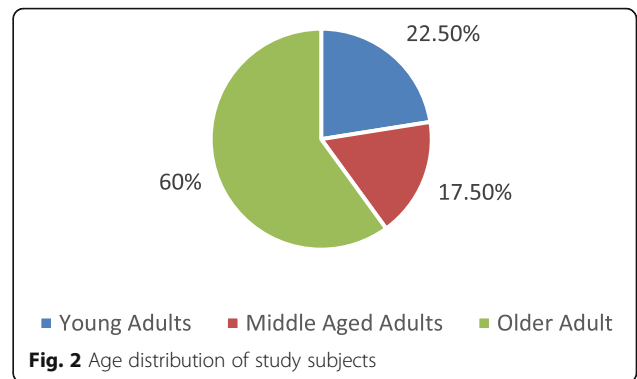
A study of the incidence, prevalence, and underlying etiology of these neurological emergencies among new onset seizures (NOS) can help predict course of treatment and prognosis.

**Methods**

This is a hospital-based cross-sectional observational study. Patients were recruited over 6 months from the emergency room and outpatient neurology clinics (from March 2018 till September 2018). One hundred and twenty patients presented by acute (within 24 h) new onset seizure (NOS) were included in this study.



**Fig. 1** Sex distribution of study subjects



**Fig. 2** Age distribution of study subjects

Inclusion criteria are as follows: All adults aged > 18 years old presented by acute new onset seizures were divided into 3 age subgroups [11]: young adult (18–35 years), middle-aged adult (36–55 years), and older adult (> 55 years).

Exclusion criteria are as follows: Patients aged < 18 years old and seizure mimics: syncope (cardiac arrhythmia, vasovagal syncope), migraine (especially presenting with isolated symptoms as vertigo, visual changes, and aphasia), vascular conditions (transient ischemic attacks), pseudoseizures/hysterical seizures, physiological nocturnal myoclonus, sleep disorders (cataplexy, narcolepsy, night terror), benign positional vertigo (BPV), and psychiatric conditions (conversion, panic attacks).

All patients were subjected to the following: Full medical and family history including past history of possible risk factors for symptomatic seizures such as diabetes mellitus (DM), chronic liver disease (hepatic encephalopathy), chronic kidney disease (CKD) or first presentation of acute renal failure (uremic encephalopathy), autoimmune diseases (such as systemic lupus erythematosus), febrile seizures, cerebrovascular accidents (CVA) including infarction and hemorrhage, head injuries as road traffic accidents (RTA), central nervous system infections (meningitis, encephalitis), and drug intake and alcohol (especially drug abuse or withdrawal).

**Family history of epilepsy**

Detailed history of the new onset seizure (type of seizure was established according to International League Against Epilepsy (ILAE) 2017 classification of seizures).

Detailed neurological examination including Mini Mental State Examination (MMSE), speech, cranial nerves examination, motor and sensory examination, and signs denoting a cause of seizure (fever, papilledema).

Laboratory investigations including complete blood count (CBC); liver function tests (LFTs), alanine transaminase (ALT), aspartate transaminase (AST), and albumin; kidney function tests (KFTs), urea and creatinine;

**Table 1** Distribution of different age groups in accordance with sex

| Gender | Age group   |        |                   |        |             |        |       |        | Chi-square     |         |
|--------|-------------|--------|-------------------|--------|-------------|--------|-------|--------|----------------|---------|
|        | Young adult |        | Middle-aged adult |        | Older adult |        | Total |        | X <sup>2</sup> | P-value |
|        | N           | %      | N                 | %      | N           | %      | N     | %      |                |         |
| Male   | 18          | 66.67  | 10                | 47.62  | 48          | 66.67  | 76    | 63.33  | 2.707          | 0.258   |
| Female | 9           | 33.33  | 11                | 52.38  | 24          | 33.33  | 44    | 36.67  |                |         |
| Total  | 27          | 100.00 | 21                | 100.00 | 72          | 100.00 | 120   | 100.00 |                |         |

random blood sugar (RBS); serum electrolytes, sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), and calcium (ionized Ca<sup>+</sup>); and others only if indicated as collagen profile, cerebrospinal fluid examination (CSF), and urine toxicology profile.

Neuroimaging including cranial computed tomography (CT) scanning with/or without contrast to identify stroke (ischemic or hemorrhagic) and space occupying lesions (SOLs) and magnetic resonance imaging (MRI) of the brain (if epilepsy syndrome is suspected), MRI was superior in identifying subtle abnormalities and remote symptomatic etiologies such as dysplasia and mesial temporal sclerosis. MRI with contrast was indicated when brain tumors or infections are suspected.

**Electroencephalogram (EEG)**

Short-term digital EEG “Nihon Kohden EEG-1200 Neurofax 2014 USA” within average 48–72 h of patient first presentation to help classify seizure type and risk of recurrent seizures.

**Statistical methods**

IBM SPSS statistics (V. 21.0, IBM Corp., USA, 2012) was used for data analysis.

Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.

The probability of error at P value 0.05 was considered significant while at P value 0.01 and 0.001 are highly significant.

**Ethical considerations**

All subjects were informed of the general aim of the study and their participation was fully voluntary. Informed written consent had been obtained and approved by the ethics committee for clinical research of the Faculty of Medicine.

**Results**

**Age and sex distribution of study subjects**

One hundred and twenty patients, presented to ER and Neurology Clinic, at the time of first ever seizure. Of patients, 63.33% were males (76) and 36.67% were females (44) (Fig. 1).

New onset seizures were more in older adult age group (60%) than in young adults (22.5%), with fewer incidences among middle-aged group (17.5%) (Fig. 2).

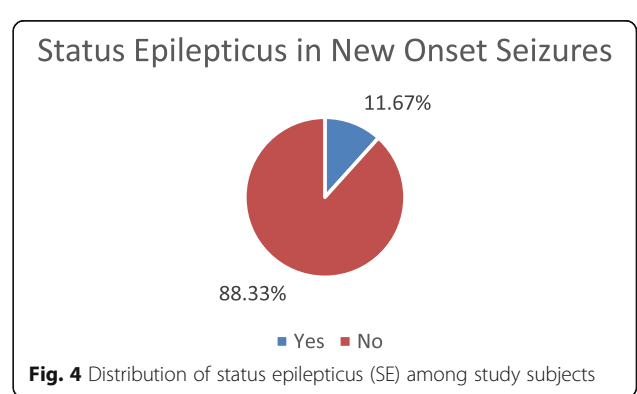
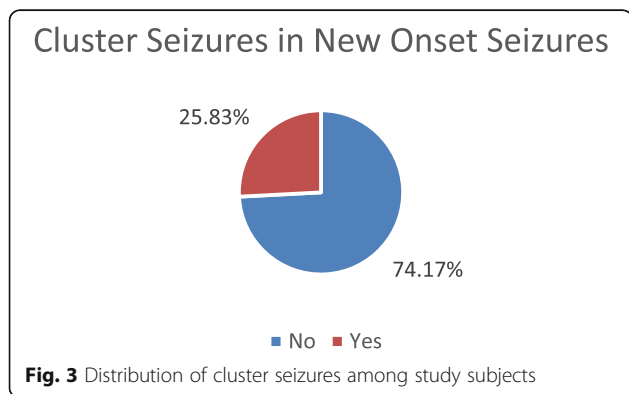
Males with new onset seizures were predominant among young and older adult age groups by 66.67%, while females with new onset seizures were predominant among middle-aged adults by 52.38% (Table 1).

**Frequency of cluster seizures and SE among new onset seizure**

Of 120 patients presented with new onset seizures, 31 (25.83%) presented by cluster seizures and 14 (11.67%) presented by status epilepticus (SE) (Figs. 3 and 4).

**Etiology of new onset seizures**

Cerebrovascular diseases were the most common identified etiology of new onset adult seizures by 47% [post-stroke epilepsy (41.67%), intracranial hemorrhage



**Table 2** Distribution of etiology of new onset seizures among study participants

| Etiology                                    | N          | %             |
|---|------------|---------------|
| Post-stroke epilepsy                        | 50         | 41.67         |
| SOL (brain tumor)                           | 11         | 9.17          |
| Idiopathic epilepsy syndrome                | 22         | 18.33         |
| Cryptogenic*                                | 6          | 5.00          |
| Encephalitis                                | 7          | 5.83          |
| Post-traumatic epilepsy                     | 3          | 2.50          |
| Acute symptomatic seizures (metabolic)      | 10         | 8.33          |
| Acute symptomatic seizures (PRES)           | 1          | 0.83          |
| Acute symptomatic seizures (vasculitis)     | 1          | 0.83          |
| Acute symptomatic seizures (drug induced)** | 1          | 0.83          |
| Traumatic SAH                               | 2          | 1.67          |
| ICHgE                                       | 3          | 2.50          |
| SDH   | 3          | 2.50          |
| <b>Total</b>                                | <b>120</b> | <b>100.00</b> |

\*Un-identified possible etiology

\*\* Opiate

SOL space occupying lesions, PRES posterior reversible encephalopathy syndrome, SAH subarachnoid hemorrhage, SDH subdural hemorrhage, ICHgE intracranial hemorrhage

“ICHgE” (2.5%), and subdural hematoma “SDH” (2.5%)], followed by idiopathic epilepsy syndrome (18.33%), symptomatic mainly “Metabolic” (11%), brain tumors (9.17%), encephalitis (5.83%), cryptogenic (5%), and traumatic and post-traumatic epilepsy (4%) (Table 2).

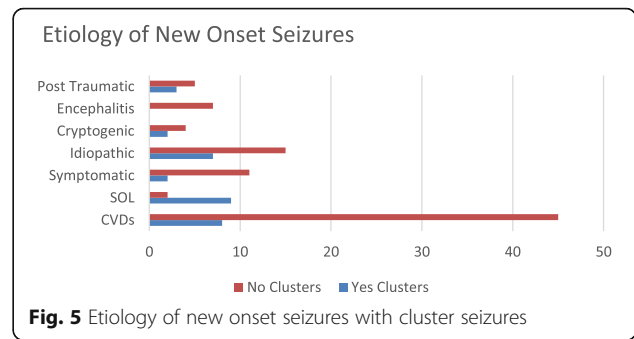
**Etiology of cluster seizures (CS)**

Of 31 patients presented with cluster seizures as first ever seizure, the most common etiology were brain tumors (29.03%), followed by cerebrovascular diseases (CVDs) (25.81%), idiopathic epilepsy syndrome (22.58%), post-traumatic epilepsy (9.68%), and symptomatic and cryptogenic etiologies by 6.45% each (P-value < 0.001) (Table 3 and Fig. 5).

**Table 3** Distribution of etiology in accordance with cluster seizures

| Etiology of new onset seizures |                              | Cluster seizures |       |     |       | Total |       | Chi-square     |          |
|--------------------------------|------------------------------|------------------|-------|-----|-------|-------|-------|----------------|----------|
|                                |                              | No               |       | Yes |       |       |       | X <sup>2</sup> | P-value  |
| Etiology                       | Cerebrovascular              | N                | %     | N   | %     | N     | %     |                |          |
|                                | SOL (brain tumor)            | 2                | 2.25  | 9   | 29.03 | 11    | 9.17  | 25.520         | < 0.001* |
|                                | Acute symptomatic seizure*   | 11               | 12.36 | 2   | 6.45  | 13    | 10.83 |                |          |
|                                | Idiopathic epilepsy syndrome | 15               | 16.85 | 7   | 22.58 | 22    | 18.33 |                |          |
|                                | Cryptogenic                  | 4                | 4.49  | 2   | 6.45  | 6     | 5.00  |                |          |
|                                | Encephalitis                 | 7                | 7.87  | 0   | 0.00  | 7     | 5.83  |                |          |
|                                | Post-traumatic epilepsy      | 5                | 5.62  | 3   | 9.68  | 8     | 6.67  |                |          |

\*Metabolic, PRES, vasculitis, drug-induced seizure



**Fig. 5** Etiology of new onset seizures with cluster seizures

**Etiology of SE**

Out of fourteen patients presented with SE, the most common etiology were CVDs (35.71%), followed by brain tumors (21.34%), symptomatic (14.29%), encephalitis (14.29%), and post-traumatic and idiopathic epilepsy by 7.14% each (Table 4 and Fig. 6).

**Discussion**

As far as we know, there were no major hospital-based studies that evaluated new onset seizures in adults especially from Egypt.

Most epidemiologic studies of seizure disorders are studies of the prevalence of epilepsy and only a few prospective incidence studies of cases with a first ever seizure in adult population exist [12].

The importance of adult onset seizures stems from its frequent association with secondary causes. If proper analysis of etiology is made with history taking, clinical examination, and appropriate investigations, the presenting seizures can be treated accordingly, thus reducing associated morbidity and mortality [13].

In 2010, the International League Against Epilepsy (ILAE) Commission for Classification of Epilepsy divided epilepsies into three categories (genetic, structural/metabolic, unknown cause) according to the etiologies of epilepsy [14].

**Table 4** Distribution of etiology in accordance with status epilepticus

| Etiology                     | Status epileptics |       |     |       |       |       | Chi-Square     |         |
|------------------------------|-------------------|-------|-----|-------|-------|-------|----------------|---------|
|                              | No                |       | Yes |       | Total |       | X <sup>2</sup> | P-value |
|                              | N                 | %     | N   | %     | N     | %     |                |         |
| Cerebrovascular              | 48                | 45.28 | 5   | 35.71 | 53    | 44.17 | 6.852          | 0.335   |
| SOL (brain tumor)            | 8                 | 7.55  | 3   | 21.43 | 11    | 9.17  |                |         |
| Acute symptomatic seizure*   | 11                | 10.38 | 2   | 14.29 | 13    | 10.83 |                |         |
| Idiopathic epilepsy syndrome | 21                | 19.81 | 1   | 7.14  | 22    | 18.33 |                |         |
| Cryptogenic                  | 6                 | 5.66  | 0   | 0.00  | 6     | 5.00  |                |         |
| Encephalitis                 | 5                 | 4.72  | 2   | 14.29 | 7     | 5.83  |                |         |
| Post-traumatic epilepsy      | 7                 | 6.60  | 1   | 7.14  | 8     | 6.67  |                |         |

\*Metabolic, PRES, vasculitis, drug-induced seizure

We evaluated the data of 120 patients presented to ER and Neurology Clinic, who were ≥ 18 years of age at the time of first seizure. Of patients, 76 (63.33%) were males and 44 (36.67%) were females with a male to female ratio of 1.7:1.

Kaur and colleagues reported mild to moderate preponderance of males, with male to female ratio (1.85:1), and Chalasani and colleagues reported the same with a ratio of 1.9:1 [12, 13].

Yet, a study done by Derle and colleagues showed that females represented 50.8% of cases [15].

This can be explained by high incidence of head trauma in young adult males and CVDs in older adult males in comparison to corresponding age category in females, while Derle and colleagues reported increasing incidence of CVDs in females after menopausal hormonal changes with > 65 years of age female preponderance [15].

Faught and colleagues concluded that the average annual incidence of epilepsy in the elderly, aged 65 years and older, is up to 240 per 100,000 [16].

Ghosh and colleagues reported that nearly 25% of new onset epilepsy occur in the elderly [17].

Joshi and colleagues reported an increased number of patients with first seizure among older age group > 60 years [18].

The increasingly aging population in the last decades and the age itself being an independent risk

factor for CVDs and the concomitant increase in the incidence and prevalence of post-stroke seizures can explain the higher prevalence of post-stroke epilepsy in our study among older age group (> 55 years) accounting for nearly 50% of our cases with new onset seizures.

On the contrary, other studies from India done by Kaur and colleagues, Chalasani and colleagues, and Muralidhar and colleagues revealed that the majority of cases were in the age group < 40 years [12, 13, 19].

Younger patients with epilepsy often show a genetic cause. However, new onset epilepsy in the elderly is mainly the consequence of accumulated injuries to the brain and other secondary factors [20].

New onset epilepsy in elderly people often has underlying etiology including CVDs, brain tumors, and traumatic head injury [21].

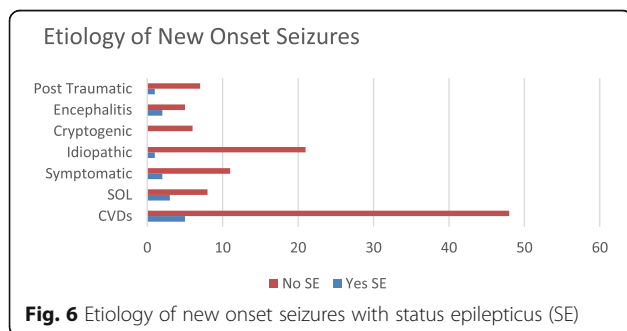
The present study highlighted the burden of new onset seizure with post-stroke epilepsy (41.67%). Therefore, better understanding of seizures’ characteristics, underlying etiological causes and drug interactions are necessary for effective patient management. As well as close follow-up of stroke patients for early detection of subtle fits which are hardly identified by patients themselves or their caregivers.

The second most common identified etiology of new onset seizures was idiopathic epilepsy syndromes (18.33), followed by SOL “Brain tumor” (9.17), acute symptomatic seizure “metabolic” (8.33%), post-traumatic epilepsy (6.67%), encephalitis (5.83%), and cryptogenic (5%).

Surprisingly, post-traumatic seizures were represented by fewer incidences than expected in Egypt.

The present study revealed that 25.83% of patients (n = 31) presented by cluster seizures and 14 (11.67%) of patients presented with status epilepticus (SE).

Chalasani and colleagues found that out of the 98 patients presented by new onset seizures above 20 years of age, 11% presented by SE [12].



**Fig. 6** Etiology of new onset seizures with status epilepticus (SE)

The current study revealed that the most common underlying etiology, in patients presented with cluster seizures was SOL “Brain Tumors” (29.03%) followed by CVDs (25.8%).

We found that out of 11 patients with SOL (brain tumors) identified etiology of new onset seizure, 9 of them (81.8%) presented by cluster seizures with highly statistically significant value ( $P$  value < 0.001).

The current study revealed that the most common underlying etiology, in patients presented with status epilepticus, was cerebrovascular (35.71%) followed by brain tumors (21.34%).

In contrast to a study done by Kaur and colleagues who reported that out of 17 patients presented with status epilepticus, the most common cause was metabolic (35.3%) [13].

## Conclusion

Cluster seizures represented 25% of new onset seizures in adult Egyptian patients. Status epilepticus is prevalent among only 11%. Despite of, CVDs are the most prevalent etiology for new onset seizures in adult population (41%) including those presented with status epilepticus (35%). However, brain tumors are the most prevalent etiology for new onset cluster seizures.

## Abbreviations

SE: Status epilepticus; CS: Cluster seizures; ER: Emergency room; NOS: New onset seizure; MMSE: Mini Mental Status Examination; EEG: Electroencephalogram; CVDs: Cerebrovascular diseases; BPV: Benign positional vertigo; DM: Diabetes mellitus; CKD: Chronic kidney disease; RTA: Road traffic accidents; ILAE: International League Against Epilepsy; SOLs: Space occupying lesions; CT: Cranial computed tomography; MRI: Magnetic resonance imaging; ICHge: Intracranial hemorrhage; SDH: Subdural hematoma

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## Authors' contributions

MH proposed the idea of the study. AK collected the data. EA revised the data. MS revised the results and wrote the manuscript. The authors have read and approved the final manuscript.

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## Availability of data and materials

From the corresponding author

## Declarations

### Ethics approval and consent to participate

All subjects were informed of the general aim of the study and their participation was fully voluntary. Informed written consent had been obtained and approved by the ethics committee for clinical research of Faculty of Medicine ASU.

Date of ethical approval: 28 December 2017.

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### Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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