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Tick-Borne Encephalitis infection among patients with neurological acute and sub-acute disorders living in Saint-Etienne area in France between 2021 and 2023

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Introduction and Aim

Tick-Borne Encephalitis Virus (TBEV) is an arbovirus transmitted through infected *Ixodes* tick bite or after ingestion of unpasteurized dairy products from infected mammals (Figure 1). Tick-borne encephalitis (TBE) is an emerging cause of nervous system infection in Europe, including France (Figure 2A). Since 2017, several sporadic cases of TBE have been reported around Saint-Etienne, in Auvergne-Rhône-Alpes (AURA) (Figure 2B). It is necessary to evaluate the local burden of this zoonotic disease to adapt our diagnosis and vaccination strategies.

To describe the epidemiology of TBE among patients presenting with acute and subacute neurological symptoms in Saint-Etienne area and surrounding between January 2021 and December 2023, and to describe the confirmed TBE cases.

Patients and Methods

This retrospective study includes patients aged over 2 years old presenting neurological acute and sub-acute disorders from 2021 January 1st to 2023 December 31st, living in Saint-Etienne and its area and for whom residual CSF specimen was stored at -80°C or if they had been tested for antibodies against TBEV in the clinical management. When available, and if CSF specimen were either positive or in not enough quantity to be analyzed, serum specimens were tested. CSF specimens were analysed for TBEV antibodies using ELISA Virion/Serion IgG and IgM kits (Eurobio, France) or CLIA kits on the Virclia® platform (Eurobio, France). The local ethic committee approved this study.

A TBE case was defined according to the European Centre for Disease Prevention and Control (ECDC) criteria [3]: a case is classified as confirmed when a patient met the clinical criteria (symptoms of inflammation of the CNS (e.g. meningitis, meningoencephalitis, encephalomyelitis, encephaloradiculitis) and at least one of the following laboratory criteria: (i) TBEV specific IgM and IgG antibodies in blood, (ii) TBEV specific IgM antibodies in CSF, (iii) seroconversion or four-fold increase of TBEV-specific antibodies in paired serum samples, (iv) detection of TBEV viral nucleic acid in a clinical specimen, (v) or isolation of TBEV virus from clinical specimen. It is also stated that serological results should be interpreted according to previous exposure to other flaviviral infections and the flavivirus vaccination status, and that confirmed cases in such situations should be validated by serum neutralisation assay or other equivalent assays. The specificity of TBEV antibodies was confirmed either by neutralisation test (NT) at Strasbourg University Hospital Laboratory (reference center for Lyme disease and TBE) and/or by a sample previously sent at the time of the clinical management at National French reference center (NRC) of Arboviruses in Marseille, France.

Results

Among them, 544 patients (42.1%) were included according to our inclusion and exclusion criteria (Figure 3). The clinical characteristics are depicted in Figure 4. The clinical diagnosis retained are summarized in Figure 5A and the etiologies in Figure 5B. Results of TBEV antibodies according to the year of clinical symptoms are detailed in Figure 6. The clinical symptoms of the 7 TBE cases are summarized in Figure 7.

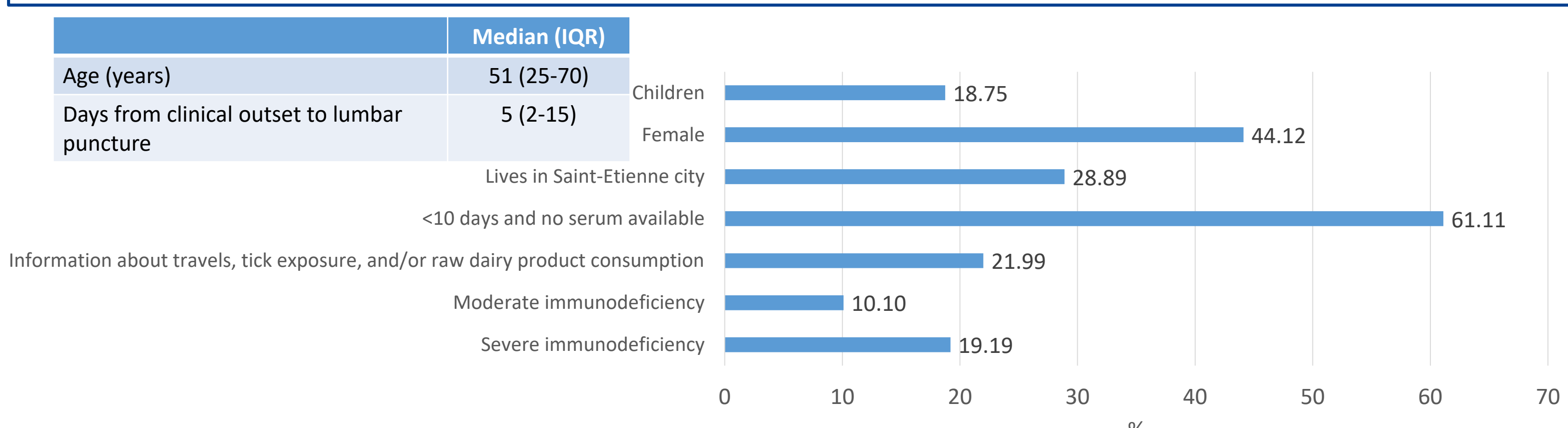


Figure 4: Main characteristics of the 544 patients included in the study.

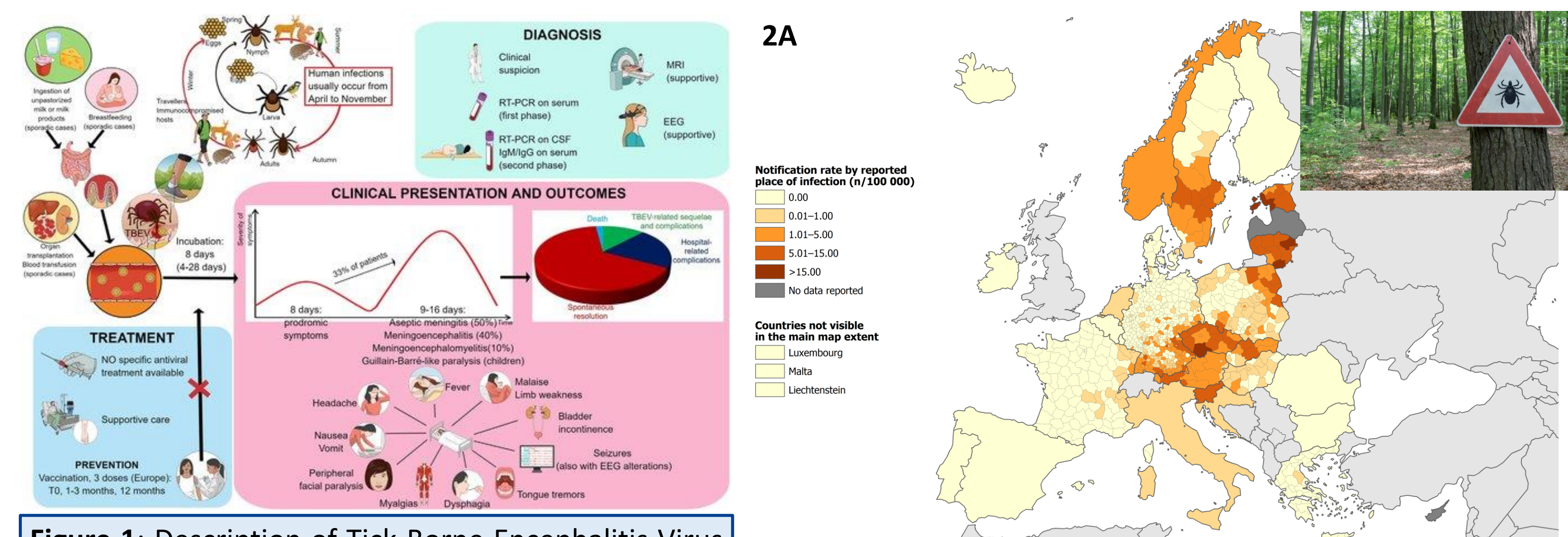


Figure 1: Description of Tick-Borne Encephalitis Virus (TBEV) transmission, diagnosis, clinical presentations, outcomes, treatment and vaccination. From [1].

Figure 2: Epidemiology of TBE in Europe (A) and in France (B). A- Notification rates of confirmed locally-acquired tick-borne encephalitis cases per 100 000 population, EU/EEA countries, 2022 (ECDC). B- Declaration of TBE cases to the French Surveillance Authorities (Santé publique France) in October 2023, with cases we published in 2017-2018 in AURA depicted by blue arrows [2].

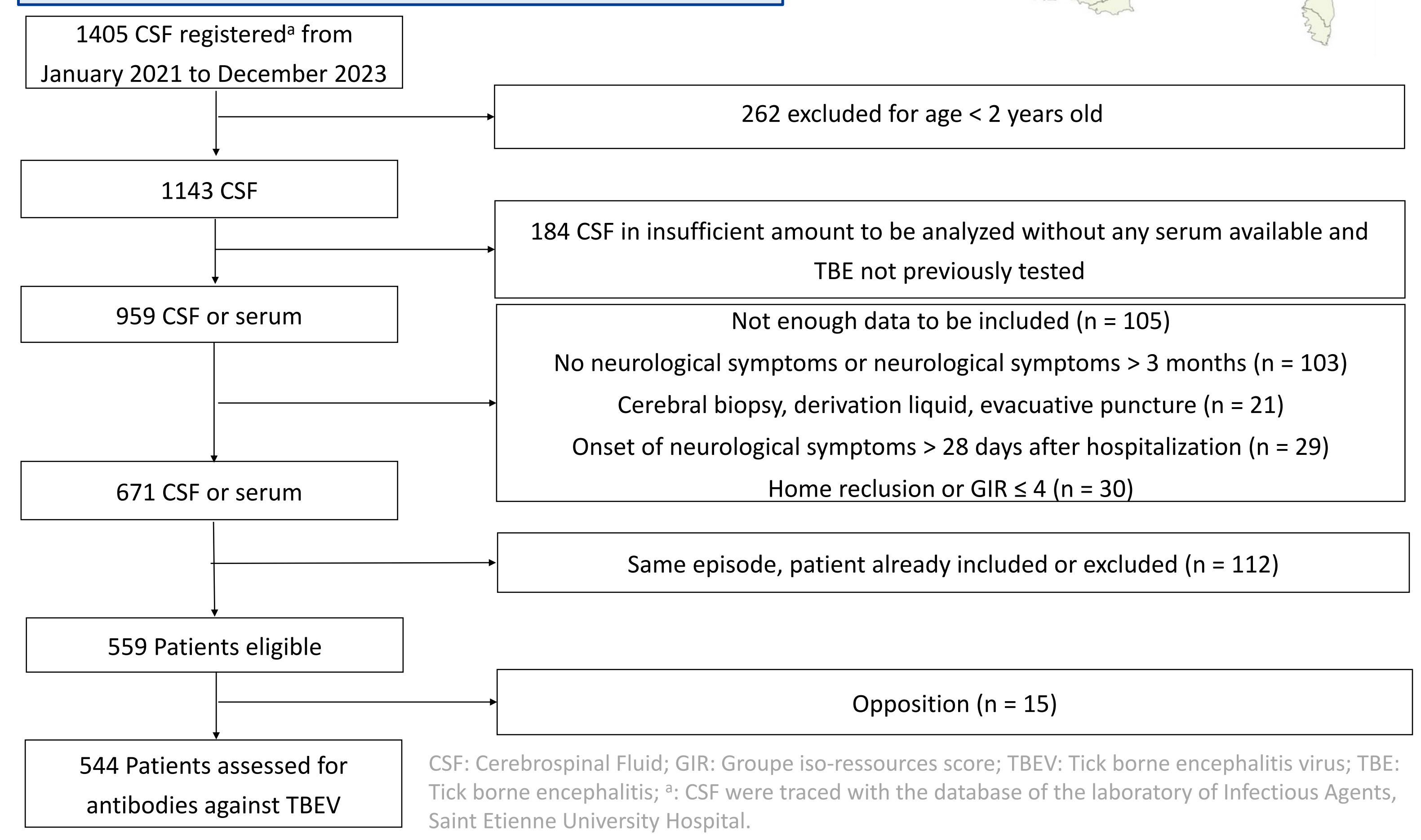


Figure 3: Flowchart of the study performed in Saint-Etienne area, France, 2021-2023.

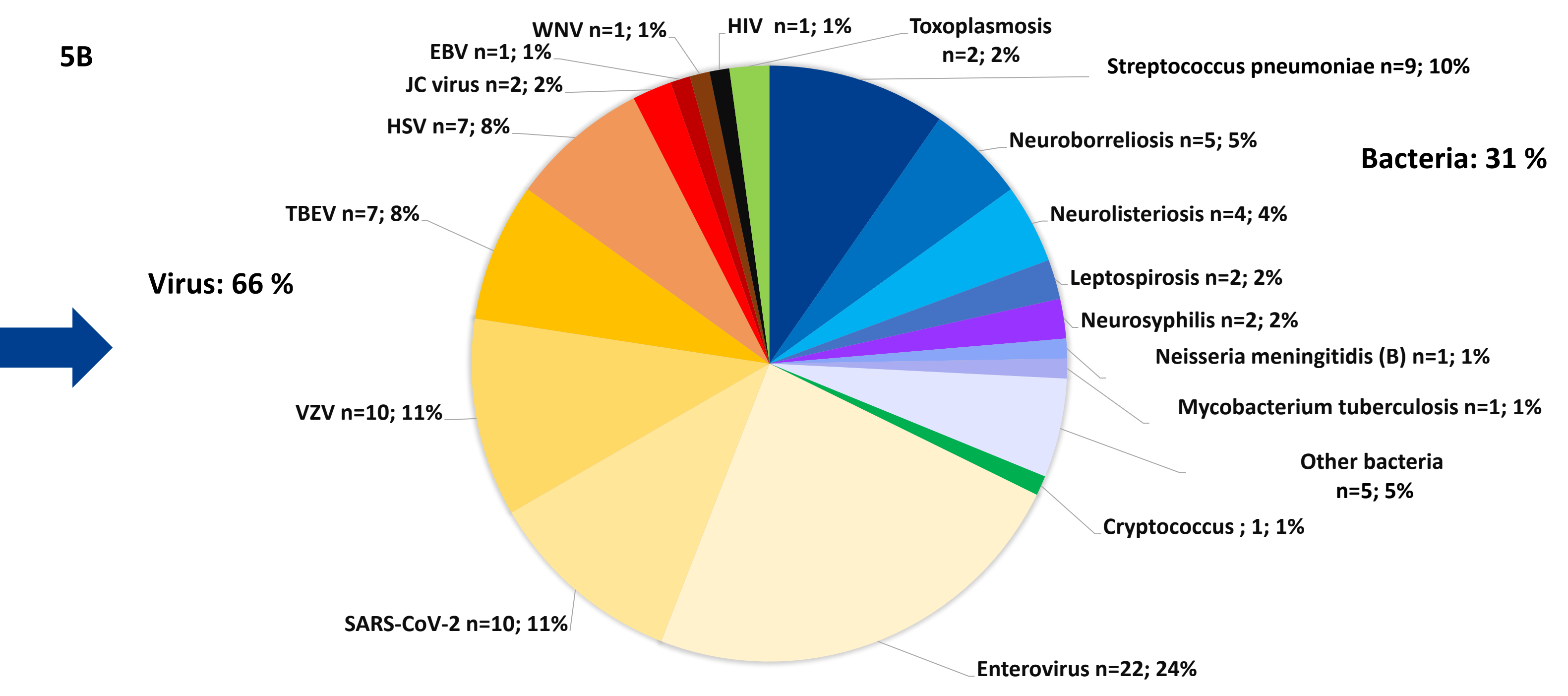
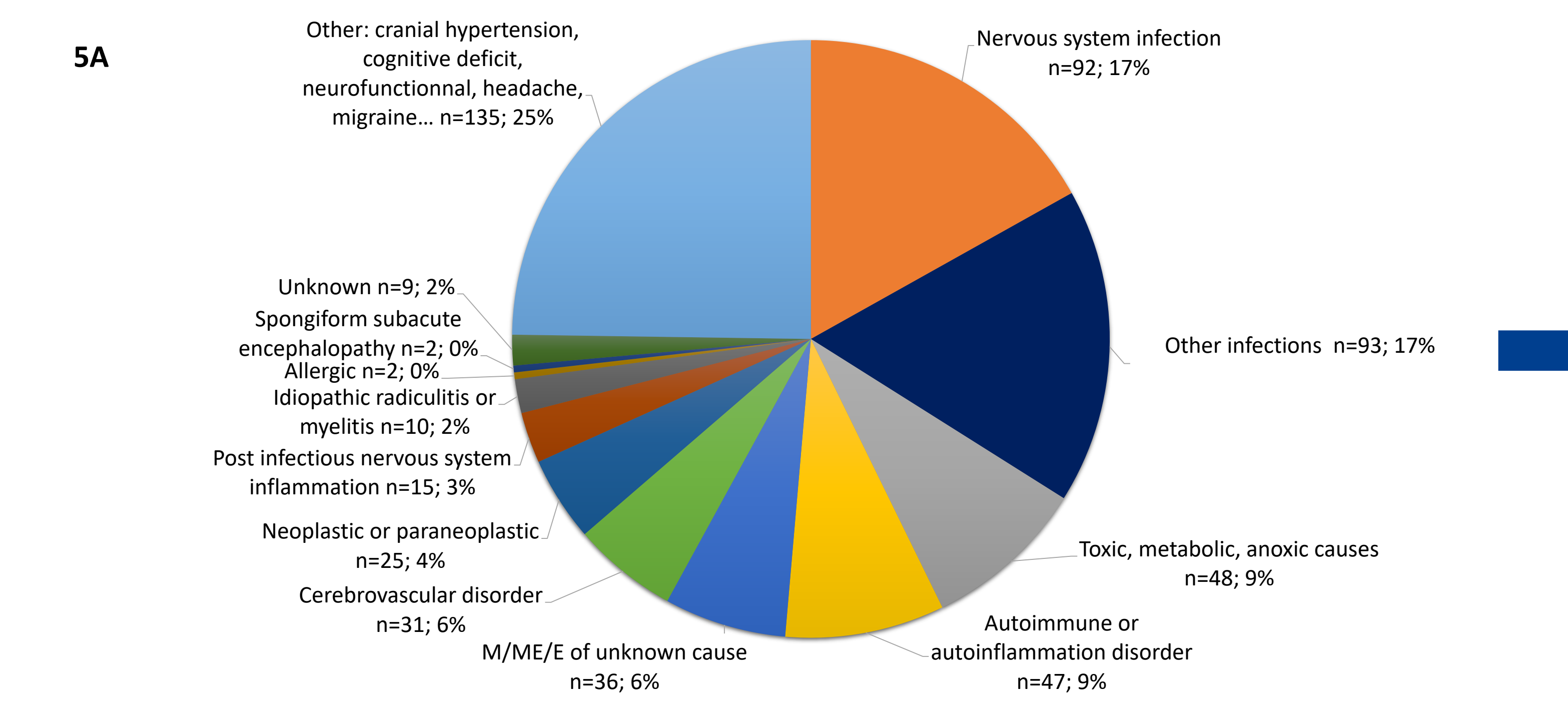


Figure 5: Main clinical diagnosis and etiologies. A- Clinical diagnosis of the 544 patients included in this study. B- Infectious etiologies of the nervous system infections (n=92).

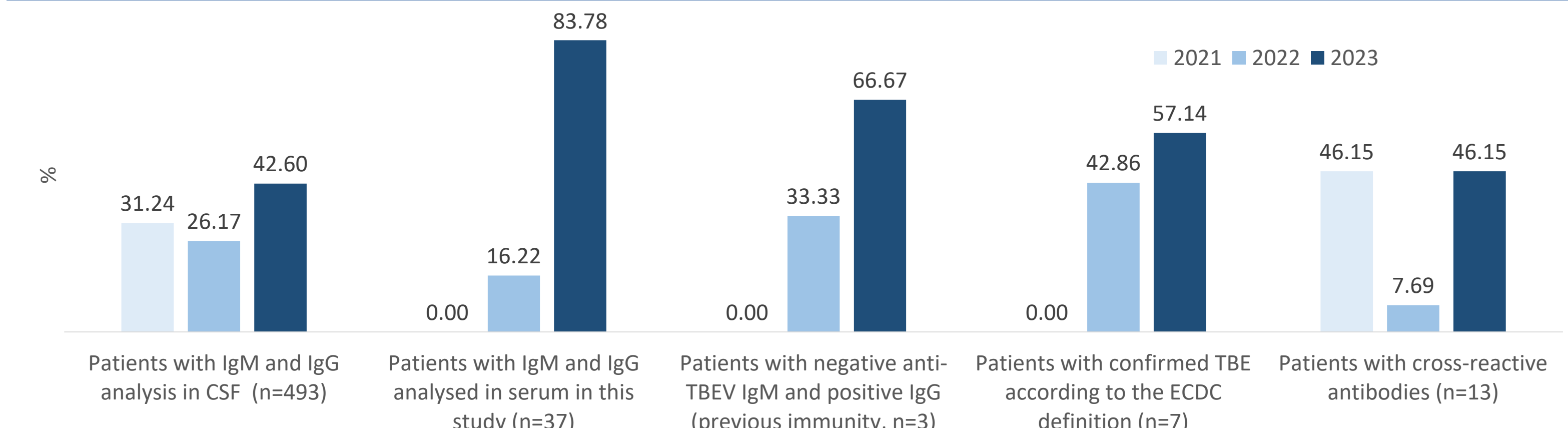


Figure 6: Antibodies against tick-borne encephalitis virus (TBEV) tested in our laboratory among patients with acute or subacute neurological signs, Saint-Etienne area and surroundings, France, 2021 - 2023, (n=544).

Discussion and conclusion

- We added 7 more cases of TBEV in AURA region since 2019 [2].
- In Saint-Etienne area and surroundings, TBEV is :
 - One of the 3 main causes of meningoencephalitis/encephalitis with HSV and VZV
 - One of the 5 first causes of meningitis/meningoencephalitis/encephalitis (9% of all infectious causes)
- We need to raise awareness among physicians for better and shorter diagnose, and among local population for prevention.
- TBEV exposure, biphasic scheme should be systematic in the anamnesis if infectious meningitis/meningoencephalitis/encephalitis is suspected in our area. TBEV research should be performed more systematically in presence of evocative neurological signs and symptoms with serology.
- In the future and if this trend is confirmed, vaccination should be considered for people living in rural/forestry area around Saint-Etienne, and people whose leisure, professional activities or dairy product consumption expose to a higher risk of TBE, especially for immunocompromised individuals and individuals over 50 years old.

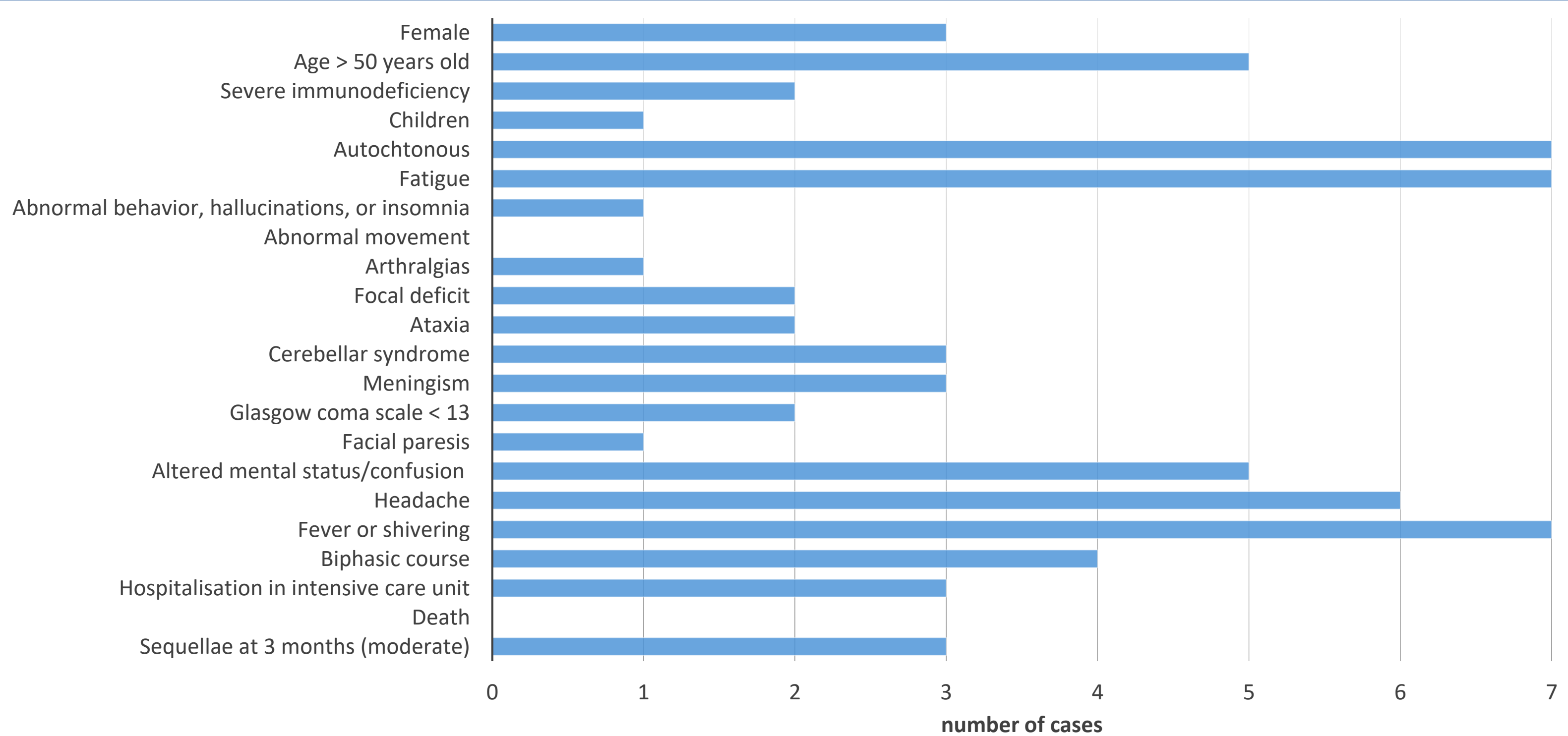


Figure 7: Clinical presentation of the 7 cases of TBE during 2021 to 2023 in Saint-Etienne area and surroundings. All the confirmed cases lived in rural areas, 5 presented with meningoencephalitis, one with meningoencephalomyelitis and one with meningitis. One patient had not been previously diagnosed for TBE. None died, and 3 were hospitalized in Intensive Care Unit (median duration 6 days range (4 - 7)).

Références

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