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Epidemiology of anti-neutrophil cytoplasmic antibody-associated vasculitis in Lithuania, 2012–2021: a retrospective cohort study

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ABSTRACT

Objectives The aim of this study was to assess the incidence, prevalence and mortality of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in Lithuania.

Design Retrospective cohort study.

Setting Lithuanian National Health Insurance Fund and Causes of Death registries, covering 1 January 2012 through 31 December 2021.

Participants Patients were identified from national healthcare registries in Lithuania. The following inclusion criteria were applied: 1) diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA), granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) (diagnosis codes M30.1, M31.3 and M31.7, according to International Classification of Diseases 10th version (ICD-10)) recorded between 1 January 2012 and 31 December 2021; 2) diagnosis of AAV was recorded in the database at least twice with at least 1-month period between the two timepoints; 3) a record of at least once prescribed reimbursed medication—glucocorticoids (prednisolone or methylprednisolone), conventional synthetic disease-modifying anti-rheumatic drugs (methotrexate, azathioprine, hydroxychloroquine and cyclophosphamide) or biological disease-modifying anti-rheumatic drug (rituximab or available biosimilars); and 4) age >18 years at the time of diagnosis.

Outcome measures Data for the analysis included sex, age, ICD-10 code of AAV, the first date of AAV diagnosis and date of death. The study period was subdivided into periods 1 (2013–2015), 2 (2016–2018) and 3 (2019–2021). Temporal trends of the incidence of AAV were assessed. Point prevalence data were recorded. Sex- and age-standardised mortality ratios (SMRs) were calculated. The life expectancy of patients with AAV was estimated by standard single-decrement life-table analysis.

Results We identified 236 patients with AAV (female, 58%) with an annual incidence of 8.22 per 1 000 000 adult inhabitants (period 1, 9.83; period 2, 6.88; period 3, 7.95). Increasing incidence was noted for MPA (period 1, 0.9; period 3, 2.49). The incidence of GPA (4.89 per 1 000 000 inhabitants per year) was three times higher than the total incidence of EGPA and MPA. The prevalence of AAV per 1 000 000 adult population increased from 35.92 in 2015 to 69.14 in 2021. 40 deaths were recorded during the study period, with a mean age at death of 65.2 (±13.03). AAV was associated with reduced life expectancy compared with the general population, especially when diagnosed at a young age. The SMRs for the total AAV cohort revealed a decreasing trend: 1.79 in period 1 and 1.67 in period 3.

Conclusions AAV is associated with increased mortality. During the study period, the incidence of AAV was found to be stable, and the prevalence has increased.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The main strength of this study is that data on all Lithuanian residents were taken from a reliable data source.
⇒ We report the incidence and prevalence of AAV from 2013 to 2021.
⇒ Patients who were not treated with reimbursed medications were not included.

INTRODUCTION

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of disorders characterised by inflammation and destruction of predominantly small- and medium-sized blood vessels and the presence of circulating ANCA, resulting in occlusive, stenotic or aneurysmal changes leading to ischaemic or haemorrhagic events.[1] The main AAV clinicopathological types are granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA).[2] The aetiology of AAV is multifactorial and influenced by genetic as well as environmental factors.[3]

The incidence of AAV has increased globally during the past 40 years; this could be related to the introduction of ANCA testing in the 1990s and improved case recognition.[4] The overall incidence rates of AAV differ geographically, ranging from 10 to 25 cases per million inhabitants in Europe. The gender distribution of AAV is similar in

Table 1 Patient characteristics

	EGPA	GPA	MPA	Total
Number of patients	45	143	48	236
Female, %	55.55	58.04	60.42	58.05
Mean age at the time of diagnosis, SD	54.87±13.85	52.05±14.33	58.92±11.54	53.98±13.93

EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

most studies, with a slight male predominance. The age-specific incidence for the whole group of AAV increases with age.[4] The pooled incidence of different AAVs in Europe was 8.5, 4.7 and 1.7 per million for GPA, MPA and EGPA, respectively.[5]

Due to an increase in incidence, improved case identification, better management, introduction of biological disease-modifying drugs and greater survival rates, the prevalence of AAV is also rising worldwide.[6] The pooled prevalence for all types of AAV is 198.0 per million,[5] ranging from 44.8 per million, in southern Spain,[7] to 421 per million, in the USA.[8] A study performed in Norway reported the increasing prevalence of AAV, where an increase from 181 per million in 2003 to 352 per million in 2013 was observed.[1 9] Regarding the prevalence of different clinicopathological types of vasculitis, the reported pooled prevalence values of different AAVs in Europe were 137.0, 35.6 and 15.4 per million for GPA, MPA and EGPA, respectively.[5]

Epidemiological results are still highly variable in Europe and the world, which may be due to regional differences in disease epidemiology, local awareness, referral practices, follow-up time and case ascertainment. Although the aetiology of AAV is still unknown, the disease burden is increasing due to increasing incidence and prevalence. Moreover, AAV is associated with high disease and treatment-related morbidity and mortality risk among patients.[10] Therefore, epidemiological studies of AAV are essential to raise awareness and promote vigilance to improve their management.

The ethnic composition of Lithuania varies, but is relatively homogeneous, as Caucasian Lithuanians clearly dominate. According to the Lithuanian Department of Statistics Official Statistics Website, in 2021, 84.6% of the country's population is Lithuanian. All specialists working in medical institutions, both public and private, are required to enter medical data into public databases, which are a comprehensive repository of healthcare data in Lithuania. The aim of this study was to estimate the incidence and prevalence rates of all clinical forms of AAV from 2012 to 2021 in Lithuania, as no comprehensive studies of AAV epidemiology and trends have been conducted in the Baltic States over the past decade. Another aim was to evaluate mortality ratios and life expectancy of patients with AAV in comparison with the general population.

METHODS

Data sources

The study was conducted using data from the public databases of the Lithuanian National Health Insurance Fund Information System SVEIDRA and the Causes of Death Register, managed by the Health Information Centre at the Institute of Hygiene.

The SVEIDRA database serves as a comprehensive repository of healthcare data in Lithuania, capturing all reimbursed physician visits, procedures, hospitalisations, diagnoses and prescribed medications in Lithuania since 1995.

The Registry of Deaths records every death and its causes (indicated in the death certificate and subsequently validated) in Lithuania and of Lithuanian citizens. Databases were linked using the Lithuanian personal code. Computerised data from the SVEIDRA database, eligible for the research, were only available from 2012 because of national regulations, requiring that data be depersonalised after 10 years. Therefore, data from separate databases cannot be merged using the personal code of the patient as an identifier of the case.

Data can be provided from these and other databases following the Lithuanian Law for Health Data Reuse.

For the purpose of this study, the researchers were provided with a list of all the patients in Lithuania with a recorded AAV diagnosis by the Lithuanian State Data Agency, operating the data from the two databases. For the verification of cases, a set of inclusion criteria was applied: (1) diagnoses of EGPA, GPA and MPA (diagnosis codes M30.1, M31.3 and M31.7 according to International Classification of Diseases 10th version (ICD-10)) recorded between 1 January 2012 and 31 December 2021; (2) diagnosis of AAV was recorded in the database at least twice with at least 1-month period between the two time points; (3) a record of at least once prescribed reimbursed medication, such as glucocorticoids (prednisolone or methylprednisolone), conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) (methotrexate, azathioprine, hydroxychloroquine and cyclophosphamide) or biological disease-modifying anti-rheumatic drug (bDMARD: rituximab with available biosimilars); (4) age >18 years old at the time of diagnosis.

Available data for the final analysis included sex, age, ICD-10 code of AAV, the first date of diagnosis of AAV and date of death, if applicable.

Table 2 Incidence of AAV

Annual incidence per 1 000 000 person-years (95% CI)	EGPA	GPA	MPA	Total
2013 to 2015	2.37 (0.37 to 7.81)	6.55 (2.54 to 13.81)	0.90 (0.02 to 5.40)	9.83 (4.68 to 18.17)
2016 to 2018	1.40 (0.09 to 6.25)	3.50 (0.84 to 9.51)	1.98 (0.24 to 7.19)	6.88 (2.74 to 14.26)
2019 to 2021	0.83 (0.01 to 5.27)	4.62 (1.41 to 11.13)	2.49 (0.41 to 7.99)	7.95 (3.42 to 15.70)
Total period	1.54 (0.12 to 6.48)	4.89 (1.56 to 11.51)	1.79 (0.18 to 6.89)	8.22 (3.60 to 16.06)

AAV, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

To look for temporal trends of the incidence of AAV, the study period was subdivided into three 3-year intervals. Period 1 encompassed 2013–2015 (patients diagnosed in 2012 were not included in the calculation of incidence because it was not possible to verify their AAV diagnosis before 2012 since no data preceding that year were available); period 2, 2016–2018; and period 3, 2019–2021. Point prevalence data were recorded at the end of each 3-year period (31 December 2015, 31 December 2018 and 31 December 2021).

The study was approved by Vilnius Regional Bioethics Committee (Approval no. 158200-17-958-462) with a waiver of informed consent.

Statistical methods

Data were analysed using the Lithuanian Health Data Reuse platform tools (Palantir Foundry). The prevalence per 1 000 000 inhabitants and crude incidence per 1 000 000 person-years were calculated for AAV in general and for specific diseases separately. As the denominator in prevalence analyses, we used the population aged ≥18 years in Lithuania at the same time points for which the prevalence was calculated (31 December 2015, 31 December 2018, and 31 December 2021). Conversely, for the analyses of incidence, data from the population aged ≥18 years in Lithuania at the beginning of each year from 2013 to 2021 were published. Data on the adult Lithuanian population were obtained from the Lithuanian Department of Statistics Official Statistics Website *Statistics Lithuania (www.stat.gov.lt)*. Owing to the low prevalence of AAV, Poisson distribution and normal approximation were used to estimate 95% CIs.

Sex-adjusted and age-standardised mortality ratios (SMRs) were calculated by dividing the observed number of deaths among patients with AAV by the expected number of deaths, the latter was calculated using national death rates from *Statistics Lithuania,* and 95 % CI for SMRs were also calculated. Life expectancy for patients with AAV was estimated by standard single-decrement life-table analysis as described by Perron *et al*.[11] Person-years of follow-up were calculated from the date of AAV diagnosis to the first date of one of the following events: death or the end of time period analysed (31 December 2021).

All statistical calculations were carried out using Microsoft Excel 2016 (Microsoft Corporation, St. Redmond, WA, USA).

Patient and public involvement

None.

RESULTS

Characteristics of patients with anti-neutrophil cytoplasmic antibody-associated vasculitis

Between 2012 and 2021, we identified 236 patients with AAV (45 patients with EGPA, 143 with GPA and 48 with MPA). The majority of the patients were female (58%), with this trend being consistent in all three disease populations and the female proportion being the largest in the MPA population (60.42%).

The mean age of the patients at the time of AAV diagnosis was 54 years, with patients with GPA being the youngest (52 years) and MPA the oldest (59 years).

Table 3 Prevalence of AAV

Point prevalence per 1 000 000 inhabitants (95% CI)	EGPA	GPA	MPA	Total
31 December 2015	8.29 (3.64 to 16.15)	24.87 (16.07 to 36.75)	2.76 (0.52 to 8.40)	35.92 (25.15 to 49.75)
31 December 2018	11.73 (6.01 to 20.62)	32.36 (22.19 to 45.60)	8.18 (3.57 to 16.00)	52.27 (39.07 to 68.50)
31 December 2021	12.83 (6.80 to 22.02)	42.41 (30.62 to 57.24)	13.90 (7.58 to 23.36)	69.14 (53.81 to 87.48)

AAV, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

Table 4 Number of patient deaths between 2012 and 2021

Year	Death cases
2012	0
2013	0
2014	2
2015	3
2016	7
2017	1
2018	7
2019	4
2020	6
2021	10
Total	40

The demographic characteristics of the study group are presented in table 1.

Incidence and prevalence of anti-neutrophil cytoplasmic antibody-associated vasculitis

The overall annual incidence of AAV from 2013 to 2021 was 8.22 (95% CI 3.60 to 16.06) per 1 000 000 adult inhabitants in Lithuania. The incidence of GPA was the highest (4.89 (1.56 to 11.51) per 1,000,000), which is about three times higher than the incidence of EGPA and MPA (1.54 (0.12 to 6.48) and 1.79 (0.18 to 6.89), respectively). Analysing the temporal trends of the incidence of AAV, we have calculated that the incidence of AAV in total did not change significantly with time. However, a trend of decreasing incidence was noted for EGPA (in 2013–2015, the incidence was 2.37 (0.37 to 7.81) and in 2019–2021, it was 0.83 (0.01 to 5.27)), and increasing incidence was noted for MPA (in 2013–2015, the incidence was 0.90 (0.02 to 5.40), and in 2019–2021, it was 2.49 (0.41 to 7.99)), although those trends were not statistically significant. The incidence of AAV in total and of different diseases is presented in table 2.

The prevalence of AAV was calculated for the three time points, and the increase in the prevalence of AAV in total is noted during the period from 2013 to 2021: the prevalence of AAV at the end of 2015 was 35.92 (25.15 to 49.75) per 1 000 000 adult inhabitants in Lithuania and 69.14 (53.81;87.48) at the end of 2021. The same trend of increasing prevalence in the second and third periods was observed for all three diseases, demonstrating that patients with AAV tend to live longer after diagnosis. GPA is the most prevalent of AAVs in Lithuania, with the prevalence at the end of 2021 being 42.41 (30.62 to 57.24) per 1 000 000. The prevalence of EGPA and MPA is more than three times lower (12.83 (6.80 to 22.02) and 13.90 (7.58 to 23.36) per 1 000 000 on 31 December 2021, respectively). The prevalence of AAV in general and of separate diseases is presented in table 3.

Standardised mortality ratios

40 death cases occurred between 2012 and 2021, of which 8 were patients with EGPA, 23 with GPA and 9 with MPA. The mean age at the time of death was 65.2 (±13.03) years. The number of death cases each year is presented in table 4. A slight increase in death cases was observed in 2021, when high mortality due to COVID-19 was observed in the general population of Lithuania.

The age- and sex-adjusted SMRs for the total AAV cohort were 1.79 (0.66 to 3.90) in the 2013–2015 period, 2.03 (1.16 to 3.30) in 2016–2018 and 1.67 (1.02 to 2.58) in 2019–2021, which includes COVID-19 pandemic years. The highest SMR was calculated for the GPA group in 2016–2018 (2.95 (1.47 to 5.29) and MPA group in 2013–2015 (2.96 (0.36 to 10.71). The SMR of patients with EGPA was the highest in 2013–2015 (2.23 (0.27 to 8.07)), with a reduction in 2016–2018, and no obvious increase in COVID-19 pandemic years (1.14 (0.23 to 3.32) and 1.16 (0.32 to 2.98), respectively). The SMR of patients with GPA decreased during the 2019–2021 period (1.87 (0.93 to 3.34) when compared with 2016–2018, but was higher than that in 2013–2015 (1.13 (0.14 to 4.07). Only mortality of patients with MPA slightly increased during the COVID-19 pandemic, with the SMR being 1.91 (0.62 to 4.45) when compared with the previous period of 2016–2018 during which the SMR was 1.34 (0.16 to 4.83), but did not reach the highest SMR, observed for this group in 2013–2015. SMRs of AAV are summarised in table 5.

Life expectancy of patients with anti-neutrophil cytoplasmic antibody-associated vasculitis

According to population census data, life expectancy for the general population in 2021 starting from the age 18–19 was 57.52 years. Patients with vasculitis, if diagnosed at age 18–19, tend to live 21 years less than the general population (figure 1). If diagnosed at the age of 70 years or older, their life span remains unchanged, presuming that vasculitis tends to be less aggressive in senior age.

Table 5 Standardised mortality ratios in the AAV cohort during different time periods

Standardised mortality ratios (95% CI)	EGPA	GPA	MPA	Total
2013 to 2015	2.23 (0.32;7.59)	1.13 (0.04;5.80)	2.96 (0.60;8.71)	1.79 (0.18;6.89)
2016 to 2018	1.14 (0.04;5.81)	2.95 (0.60;8.69)	1.34 (0.08;6.15)	2.03 (0.25;7.27)
2019 to 2021	1.16 (0.05;5.85)	1.87 (0.20;7.02)	1.91 (0.21;7.08)	1.67 (0.15;6.69)

EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis ; MPA, microscopic polyangiitis .

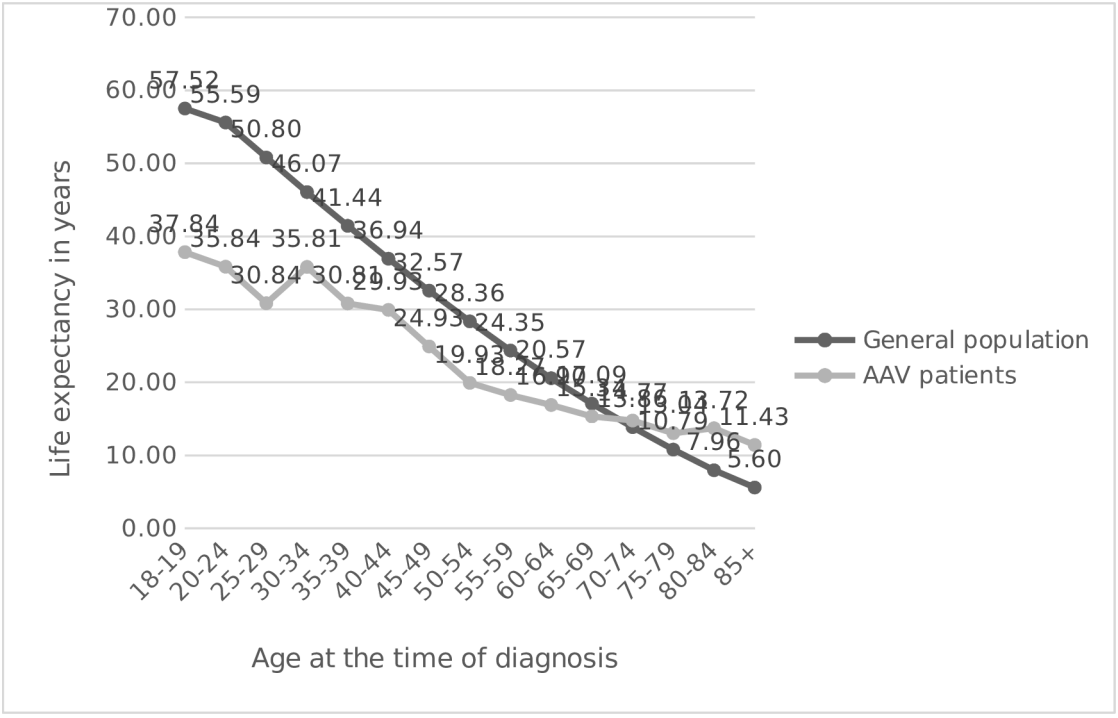

Figure 1 Life expectancy of patients with AAV in comparison with the general population in the 2013–2021 period. The life expectancy for the general population in 2021 starting from the age 18–19 was 57.52 years. Patients with vasculitis, if diagnosed at age 18–19, tend to live 21 years less than the general population. If diagnosed at the age of 70 years, their life span remains unchanged. AAV - anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

DISCUSSION

This study was conducted to evaluate epidemiological data on AAV in general and on different clinicopathological types of AAV in Lithuania. The only previous attempt to assess the epidemiology of AAV in Lithuania was made in 2005. Dadoniene *et al* reported the annual incidence of GPA to be only 2.1 per million inhabitants from 1990 to 1999.[12] Unfortunately, AAV cases were underestimated because only cases diagnosed in tertiary clinical centre were included, with a histological examination rarely carried out and the ANCA test only introduced into daily clinical practice after 1995.

In this study, 236 patients with AAV were recorded between 2012 and 2021. Although previous studies have shown that AAV is more common in men than in women and the peak incidence of vasculitis is in the 60–79 age group,[13] the majority of the patients were female (58%), with the highest proportion of women in the MPA group (60.42%). In addition, given the younger age of patients at disease onset, the average age of patients at the time of AAV diagnosis was 54 years, patients with GPA being the youngest (52.05±14.33 years) and those with MPA being the oldest (58.92±11,54 years). The same trend of older age of patients at the time of MPA diagnosis compared with GPA was confirmed in a study by Nilsen *et al* performed in Norway.[9] A possible explanation of patients with AAV being younger at the time of diagnosis in Lithuania could be that the disease onset is less severe in older age, and older patients are overlooked, not referred to rheumatologists and are instead treated by general practitioners or other specialists, such as nephrologists, with their concomitant diseases being held responsible for their symptoms.

We report the incidence and prevalence of AAV from 2013 to 2021. The total incidence of AAV in Europe and North America is approximately 20 per million per year.[3] Studies from 1998 to 2015 reported the combined annual incidence rate for AAV to be 10.2 per million inhabitants in northern Germany (1998–1999),[14] 12.2 (1998–2001) in north-western Spain,[15] 18.5 (2000–2015) in Denmark,[16] 20.4 in the UK (1988–1997),[17] 20.8 (1997–2006) in Sweden,[18] 24.7 (1999–2013) in Norway[9] and 33.0 in the USA (1996–2015).[8] However, during the period analysed in this study, the total incidence of AAV was 8.22 per million inhabitants, which might indicate that AAV is still underdiagnosed in Lithuania or suggest the importance of unidentified geographical, environmental or demographic factors that could predispose granulomatous inflammation. The incidence of separate AAV entities in Lithuania is also among the lower ones reported in Europe. Studies in Europe show annual incidence rates of 2.1–14.4, 2.4–10.1 and 0.5–6.8 per million for GPA, MPA and EGPA, respectively,[19] whereas for Lithuanian data, the estimates of overall incidence are as follows: 4.89 (1.56 to 11.51) in GPA, 1.54 (0.12 to 6.48) in EGPA and 1.79 (0.18 to 6.89) per million in MPA. The geographical trend, revealing that MPA is more prevalent in the Mediterranean area,[15] and GPA – in Northern

Europe – was previously noted and explained by the association of GPA with the HLA-DPB1*0401 allele.[20] The prevalence of the allele in the Lithuanian population has never been estimated; however, our estimated incidence ratio of GPA:MPA is 2.7:1, which is close to what has been reported in other Northern countries, as previous studies in Northern Europe have shown a GPA:MPA ratio of 3–4:1,[21 22] and more recent studies in Norway have reported a ratio of 2.3:1.[9] Previously reported data refer to an increase in the incidence of MPA with time. Likewise, in this study, the incidence of MPA increased from 0.9 in 2013–2015 to 2.49 in 2019–2021. On the contrary, the incidence of AAV in total did not change significantly during the study period, supporting the results of previous studies revealing a stabilisation of the incidence.[6]

The estimated prevalence of AAV in Lithuania is lower than the reported prevalence of AAV in Europe. The prevalence of AAV in Lithuania at the end of 2015 was 35.92 per million adult inhabitants and 69.14 at the end of 2021 compared with 352 per million in 2013[9] in Norway or 428.4 per million in 2020 in Sweden.[6] Regarding the prevalence of clinicopathologic types of vasculitis, reported prevalence values for GPA, MPA and EGPA in Norway were 261.0, 58.2 and 32.9 per million inhabitants in 2013,[9] compared with 24.87, 2.76 and 8.29 per million, in Lithuania in 2015 and higher numbers of 42.41, 13.90 and 12.83 per million in 2021, respectively. According to studies, the prevalence of EGPA is generally lower than that of GPA or MPA, with a peak estimate of 45.7 per million population[23] . This trend was also confirmed in our study.

We estimated the increase in AAV prevalence between 2013 and 2021, demonstrating that the survival of patients with the diseases is improving. Our results support the previous trend reported from Norway, where an increase in AAV prevalence in general and separate diseases was noted in 1999–2013 and was explained as a consequence of better diagnostic tools, increased survival and increased incidence. [10] We have found a slight increase in the mortality rate in the cohort of patients with AAV compared with the general Lithuanian population. The age-adjusted and sex-adjusted SMRs for the total AAV cohort were calculated to be 1.79 in 2013–2015, 2.03 in 2016–2018 and 1.67 in 2019–2021. The highest SMR was calculated for the GPA group in 2016–2018 with 2.95 and the MPA group in 2013–2015 with 2.96. The observed overall SMR in our study is close to 2.7, which was previously reported in a meta-analysis covering the period from 1966 to 2009[24] or 2.3, reported in a study in the USA in 2002–2017,[25] whereas the calculated SMR in Australia was higher, at 3.3 in 1980–2014.[26] Overall, our results support a slight reduction in the risk of mortality and an improvement in the survival of patients with AAV. Conversely, we confirm that AAV is a life-threatening disease, as we found that patients with vasculitis, if diagnosed at age 18–19 years, live for 21 years less than the general population. Inconsistency occurred when analysing mortality in the elderly. In this study, the life expectancy of patients with AAV if diagnosed at age 70 years or older remains the same as the general population, which could indicate that vasculitis is less aggressive in older age. The findings contradict the results of previous studies that have found an association of mortality risk with older age in patients with AAV.[27] This discrepancy may be explained by the fact that older patients with AAV, as well as the entire population, are at higher risk of mortality in general. Besides, they have more comorbidities influencing the overall mortality risk.

The main strength of this study is that we have taken data on all Lithuanian residents from a reliable source of information. Specialists working in private practice or private medical institutions were not obliged to enter data into these databases, but this should have little to no negative effect on our findings, as the usual practice in Lithuania is to refer patients for the verification of AAV diagnosis and conduct biopsies and immunological testing in tertiary centres of rheumatology that are state medical institutions. Only patients with very mild disease who are not treated with reimbursed medications could be omitted, which is unlikely, because glucocorticoids are widely used for these diseases and are reimbursed in Lithuania. Another explanation for the underestimation could be the high number of comorbidities, not all diagnoses were included in the database. As the personal identification code was not possible to obtain because of personal data protection rules in Lithuania, we could not verify the cases by retrieving associated medical documentation. Nevertheless, we believe that the defined inclusion criteria allowed us to reliably detect all patients with AAV in Lithuania. To our knowledge, this study is the first complex study on AAV epidemiology and its trends over the last decade in the Baltic states and East European region.

CONCLUSION

AAV is a multisystem life-threatening disease associated with an increased mortality risk. The incidence of AAV in Lithuania was found stable during the period from 2013 to 2021, whereas the prevalence has increased, which might indicate better management and treatment of patients with AAV resulting in improved survival. However, the established incidence and prevalence rates in Lithuania are among the lowest in Europe, which indicates that the disease is likely to be underdiagnosed. The mortality rate in patients with AAV has increased compared with the general Lithuanian population, and patients with AAV tend to have reduced life expectancy, especially when diagnosed at a young age.

Contributors JD designed the study and the analytical strategy and helped interpret the findings. GD conducted the literature review, helped on data analysis and interpretation, and assisted in preparing the first draft of the manuscript. GG helped on data analysis and interpretation and assisted in preparing the first draft of the manuscript. DM directed the study's implementation and helped in data interpretation. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. DM is the guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Vilnius Regional Bioethics Committee (approval number 158200-17-958-462, 7 November 2017). The participants of this study did not give written consent for their data to be shared publicly. This study received a waiver for an informed consent form being signed by participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. The participants of this study did not give written consent for their data to be shared publicly. This study received a waiver for an informed consent form being signed by participants. The document granting permission to conduct the study without informed consent may be added upon request.

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