LADDER Database

RTI INTERNATIONAL

RESEARCH REPORT

Published February 2025

RESEARCH SUMMARY

Community-Sourced Reporting of Mortalities in Angelman Syndrome (1972-2022)

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WHAT WAS THE RESEARCH ABOUT?

Until 2018, the absence of a unique diagnosis code (i.e., ICD-10 code) for Angelman syndrome (AS) limited comprehensive data on its incidence, prevalence, and mortality rates. Without an understanding of mortality patterns and risks, implementing preventative measures and appropriate medical and behavioral interventions to extend life expectancy in AS has been challenging. To address this gap, an initiative leveraging community-sourced data was launched, utilizing social media, natural history studies, and registry data to better understand the causes of death in individuals with AS.

WHAT DID THE RESEARCH TEAM DO?

Data were collected from social media, community-based sources, the Angelman Syndrome Natural History Study (NHS), and the Global AS Registry to investigate causes of death in individuals with AS. A comprehensive descriptive analysis was conducted to summarize demographic characteristics and causes of death. Age categories were defined based on known AS phenotypes, considering seizure onset and stability across different life stages.

WHO WAS IN THE STUDY?

Information was gathered about 220 individuals regarding their cause of death across nineteen countries of residence. Of those, the majority (n = 186) were reported from five English-speaking countries: the United States (n = 141), the United Kingdom (n = 17), Canada (n = 14), Australia (n = 10), and New Zealand (n = 4). Seventeen deaths were reported from Spanish-speaking countries:

Spain (n = 5), Argentina, (n = 5), Mexico (n = 3), Chile (n = 2), and one each from Cuba and Peru. Seven deaths were reported from France, two each from Germany, Ireland, and Italy, and one death each reported from Indonesia, China, Poland, and Switzerland.

WHAT DID THE RESEARCH TEAM LEARN?

Between 1979 and 2022, 220 deaths were reported in the AS community, with an average of 14 deaths annually since 2013. The reported deaths occurred across various age groups, with a median age of 18 years.

Overall Causes of Death

The leading causes of death were pneumonia/ respiratory illness (32 deaths), accidents (28), seizures (23), sudden unexpected death in sleep (SUDS) (17), and cancer (17).

Children (Ages 1-5 years)

Seizures and accidents were the leading causes of death, with notable accidents including drowning, suffocation, and choking. SUDS occurred in 7% of the cases.

Children (Ages 6-12 years)

Accidents (mainly drownings) were the leading cause of death, followed by seizures and SUDS. Cancer and postoperative complications also contributed.

Adolescents (Ages 13-18 years)

The leading causes of death were SUDS (25%), pneumonia, and accidents (including house fire and heat stroke). Four deaths were due to postoperative complications, and three were attributed to filicide.

Young Adults (Ages 19-29 years)

Respiratory illnesses, including pneumonia, were the most common cause of death, followed by seizures and accidents.

Adults (Ages 30+ years)

Cancer was the leading cause of death (particularly colorectal and lymphocytic leukemia). Pneumonia and SUDS also contributed. There was one accidental death due to a fall, and a few deaths were due to organ failure, heart failure, or neurodegeneration.

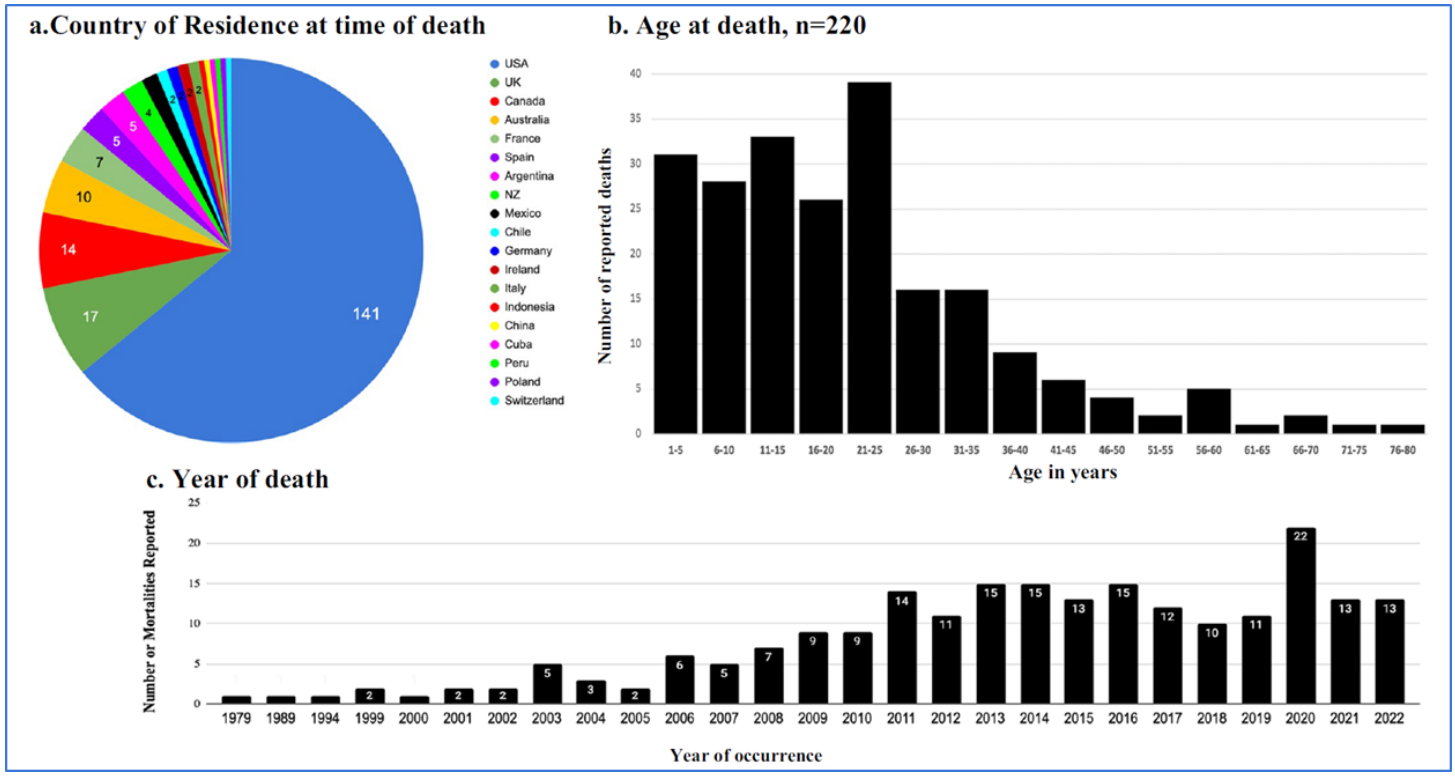

TABLE 1 | Reported causes of death in people with Angelman syndrome, by age group.

Cause of death	Ages 1–5	Ages 6–12	Ages 13–18	Ages 19–29	Ages 30+	Totals
Pneumonia/respiratory illness	3	5	5	14	5	32
Accidents	6	13	3	5	1	28
Seizures	7	5	0	9	2	23
Sudden unexpected death in sleep (SUDS)	2	3	5	3	4	17
Cancer	0	2	0	5	10	17
Post-operative complications	1	2	4	4	0	11
Homicide (Filicide)	1	0	3	2	0	6
Sepsis	0	2	2	0	0	4
Meningitis	0	2	0	0	0	2
Heart failure	0	1	0	0	1	2
COVID-19	0	0	0	1	1	2
Renal failure	0	0	0	0	2	2
Bowel perforation/obstruction	0	0	0	0	2	2
Unexpected death	0	0	1	0	0	1
Pancreatitis	0	0	0	0	0	0
Neurodegeneration	0	0	0	0	1	1
Pulmonary fibrosis	0	0	0	0	1	1
Unspecified illness	0	1	2	4	4	11
No cause listed	11	9	5	16	17	58
Totals	31	45	30	63	51	220

WHAT DOES THIS MEAN FOR FAMILIES?

This study provides early insights into the causes of death in individuals with AS, underscoring the need for more systematic exploration of morbidity and mortality risks in this population. As the unique diagnosis code for AS (ICD-10: Q93.51) becomes more widely applied in hospitalization records and death certificates, opportunities for more rigorous epidemiological study will expand. Additionally, if AS is included in newborn screening programs, true incidence and prevalence can be established, allowing for a clearer understanding of its associated mortality risks.

While some causes of death in individuals with AS overlap with those in the general population —such as cancer and accidental injuries—other risks, such as SUDS and pneumonia, may be uniquely influenced by AS-related factors.

Notably, pneumonia in AS may be linked to silent aspiration, emphasizing the need for greater awareness of swallowing difficulties and choking risks. These insights can inform early interventions and preventative strategies, ultimately supporting individuals with AS in living healthier lives.

Importantly, the median age at death reported in this study should not be interpreted as the expected lifespan of individuals with AS. Historically, many adults with AS were never diagnosed, and their families were not connected through social media or other networks, leading to an underreporting of deaths in older individuals. However, the presence of multiple individuals over 70 years old in this study suggests that there are many more elderly adults with AS worldwide.

This highlights the importance of improving identification and long-term tracking of individuals with AS to better understand their lifespan and health outcomes.

Full article by Dr. Gomes and colleagues:
Read here

Gomes, A. T., Moore, A., Cross, M., Hardesty, C., David, K., Sampedro, M. G., Dube, S., Weil-Chalker, S., Montepagano, A. G., Christel, U., Martin, R., Wheeler, A., Tan, W.-H., Bird, L. M., & Bichell, T. J. (2024). Community-Sourced Reporting of Mortalities in Angelman Syndrome (1979-2022). American Journal of Medical Genetics. Part A, e63961. https://doi.org/10.1002/ajmg.a.63961