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Outbreak investigation

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Emergence of anthrax in Bududa District, Eastern Uganda, February - May 2022: Implications for prevention and control

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Abstract

On 20 May, 2022, the Uganda Virus Research Institute confirmed the first reported anthrax outbreak in Bududa District following reports of sudden cattle deaths and suspected human cases in four adjacent villages. The Ministry of Health through the Public Health Fellowship Program immediately deployed a multi-disciplinary team led by an Epidemiologist, to determine the outbreak scope, identify risk factors, and recommend control measures. The investigation included active case finding using a standardized case definition, medical records review, a retrospective cohort study, and laboratory investigations. Laboratory tests confirmed Bacillus anthracisin both human and animal samples and in environmental soil samples. A total of 21 human case-patients (15 suspected, 6 confirmed) were identified, 17 cases among livestock (13 suspected, 4 confirmed), and 2 positive soil samples. The investigation confirmed that the outbreak was predominantly of the cutaneous form, and linked to handling and consumption of meat from infected animals. We recommended prophylactic measures for exposed individuals, enhanced surveillance, vaccination of livestock, and further epidemiological studies among animal populations. Vaccination of livestock was conducted, health education and community sensitization, and outbreak findings presented to national and district authorities. As a result, the government imposed a ban on the sale and movement of livestock in Bududa and neighboring districts in a bid to contain the outbreak.

Introduction

Anthrax manifests itself in humans in four forms: cutaneous, gastrointestinal (GIT), inhalational, and injectional, depending on the route of exposure. The cutaneous form, with an average incubation period of up to 7 days, accounts for 95% of anthrax cases reported globally and mostly occurs in Africa [1,2]. Worldwide, approximately 20,000-100,000 cases of human anthrax are reported annually [3]. While the global burden on animals is poorly documented, it has been estimated that a total of 1 billion livestock live in high-risk areas [4].

In Uganda and the neighboring East African countries, anthrax is recognized as one of the highest-ranking priority zoonotic diseases, based on a systematic assessment of socioeconomic impact, epidemic potential, and severity of disease [5-8]. Despite this, sporadic outbreaks continue to occur and are generally poorly documented, leading to underestimation of the true burden [9]. The first documented occurrence of anthrax in Uganda is at least 1918 [10]. According to the outbreak inventory housed at the Uganda National Public Health Emergency Operations Center (NPHEOC), a total of 13 outbreaks were reported in humans and 16 in animals between 2013 and 2022. In 2018, anthrax appeared for the first time in Eastern Uganda, particularly in the Kween District [11], and since then, there have been recurrent outbreaks reported in that region. Worse still, there is no policy in place regarding routine vaccination against anthrax in animals, meaning the costs of vaccination are privately met [12].

On 16 May 2022, the District Health Officer (DHO) of Bududa District, Eastern Uganda informed the Uganda Ministry of Health (MoH) of cattle that died suddenly, and suspected cases among humans in four adjacent villages. Samples were collected and shipped to the Uganda Virus Research Institute (UVRI), which confirmed the outbreak on 20 May 2022, marking the first confirmed anthrax outbreak in Bududa District. The district is located on the slopes of Mt. Elgon, approximately 257 kilometers from the capital city, with an estimated population of 210,173 and an annual growth rate of 4.5% [13]. A team comprising epidemiologists, medical doctors, and a veterinarian was deployed to investigate. We investigated to determine the scope and magnitude of the outbreak, identify exposures leading to infection, and recommend evidence-based control measures.

Methods

Case definition: we defined a suspected cutaneous anthrax case as the onset of skin lesions (papule, vesicle, or eschar) in a person residing in Bududa District from January - May 2022. A suspected gastrointestinal anthrax case was the onset of abdominal pain and at least one of the following: diarrhea, vomiting, lymphadenopathy, pharyngitis, and oropharyngeal lesions in a person residing in Bududa District from January - May 2022. A confirmed human anthrax case was defined as a suspected case that is laboratory-confirmed by isolation of *Bacillus anthracis*from an affected tissue or site, or any other laboratory evidence of *Bacillus anthracis*infection based on at least two supportive laboratory tests. We defined a suspected animal anthrax case as the sudden death of an animal in Bududa District from January - May 2022. A probable animal anthrax case was defined as a suspected case with unclotted blood emerging from body orifices in Bududa District from January - May 2022. A confirmed animal anthrax case was defined as a demonstration of gram-positive rod-shaped *Bacillus anthracis*from blood or tissue.

Case finding: the investigation was conducted between May 20th- June 6th2022. We reviewed medical records at the two health facilities serving the affected villages: Bunamono Health Centre III and Namaitsu Health Centre II, to identify human cases. Additionally, with the help of Bududa District Health and Veterinary Officials, and village health teams (community health workers), we conducted an active community search in the villages to identify human and animal cases. We modified the MoH anthrax case investigation form [14] to include relevant exposures and accommodate the case definition. Following this, we generated a line list of case-patients.

Hypothesis generation: we first interviewed all identified case patients and asked about various exposures to animals from January to May 2022 in Bududa District. These included eating meat from an animal that died suddenly, cooking it, and participating in butchering (touching meat/body fluids, carrying sick/dead animals, removing animal organs, touching skin/hides, slaughtering animals, had wounds, found dead animal remains in the garden and did soil related work).

Retrospective cohort study: we conducted a retrospective cohort study in villages located in the more affected sub-county, Bunatsami, where 90% of the cases occurred. We chose to do a cohort study because the affected villages had small populations (total of 441) and all households were easily accessible. We interviewed 216 persons from 89 households, who were present at the time of the outbreak. Furthermore, we used a structured questionnaire to gather data on demographic characteristics, symptoms, and potential exposures (touching meat/body fluids, carrying sick animals, removing animal organs, touching skin/hides, slaughtering, skinning, presence of a wound at the time of contact, doing soil related work, cooking meat from a sick animal and, eating meat). We collected data using KoboToolbox, an open-source electronic platform. All household members were eligible for inclusion. For respondents aged 7 years and below, we spoke to the parents on their behalf. To measure the associations between exposure variables and illness status, we estimated risk ratios (RR) and their 95% confidence intervals. We conducted additional common reference group analysis for the statistically significant factors. The significance threshold was at 0.05. Using population data obtained from the Uganda Bureau of Statistics [13] and community health workers of the affected villages, we computed attack rates (ARs). We used Epi info (version 7.2.5.0) and Stata (version 13) for analysis, and QGIS (version 3.2.2) to draw maps. There was no missing data.

Laboratory investigations: we collected 30 human samples and four animal samples, for laboratory analysis by the Uganda Virus Research Institute and the National Animal Disease Diagnostics and Epidemiology Centre (NADDEC), respectively.

Environmental investigations: we collected two soil samples from the premises of two farmers who reported sudden deaths of cattle, for laboratory analysis. We also observed the affected area for any factors that could be associated with the introduction of anthrax in the area and its further transmission.

Ethical considerations: this investigation was in response to a public health emergency and was, therefore, determined to be non-research. The US CDC Center for Global Health, also determined that this activity was not human subject research, and its primary intent was public health practice or a disease control activity. All methods were performed by the approval and administrative clearance without any ethical breach. We obtained informed verbal consent from respondents aged at least 18 years old; assent from children below 18 years of age who were not emancipated, and informed verbal consent from their parents or guardians. For respondents aged 7 years and below, we spoke to the parents on their behalf. The data was collected with no identifying information and stored on a password-protected computer, only accessible to the study team.

Results

Descriptive epidemiology: we identified a total of 21 case patients, 15 (71%) of whom were suspected and six (29%) confirmed (Overall AR: 10/100,000), including one death in a 55 year-old-male (CFR: 5%). Deaths among animals occurred from 14 February - 22 May 2022 while onset among case-patients occurred from 10 March - 27 May 2022 (Figure 1). Death among animals precedes the onset of the disease among humans; all 21 case-patients reported exposure to animals that died suddenly. The first two case patients, with onsets on 10 and 13 March 2022 respectively, are a skinner and butcher who both worked at an abattoir in the Bushika market and routinely handled meat from several sources. The affected villages are primarily served by that market, and it receives animals from Kenya. The median age was 26 years (range: 5-72), 16 (76%) were male and were more affected (3 per 1,000) than females. Fourteen (67%) case-patient's occupation was related to livestock. All case patients had a history of either contact with or eating meat from an animal that died suddenly.

Clinical manifestations of human case-patients: the case patients presented with signs and symptoms suggestive of either cutaneous only (12/21, 57%), GIT only (4/21, 19%), or a combination of both forms of anthrax infection (5/21, 24%) (Figure 2). Upon stratification by anthrax type, an eschar (12/12, 100%) and skin swelling (10/21, 83%) were the most common symptoms among the 12 cutaneous-only case patients. All four GIT-only case patients presented with abdominal pain and non-bloody diarrhea (4/4, 100%), and malaise (3/4, 75%). All case patients that had both forms of anthrax presented with fever, malaise, and skin swelling (5/5, 100%); followed by abdominal pain and non-bloody diarrhea (each at 4/5, 80%).

Clinical manifestations of animal cases: we identified a total of 17 suspected animal anthrax cases from seven villages in the two sub-counties reporting human cases; Bunatsami (16/17, 94%) and Nangako town council (1/17, 6%). Two out of the 17 were subsequently confirmed positive by NADDEC; All 17 animals died within a day of onset of illness (CFR: 100%) while 8/17 (47%) had blood oozing from orifices; 7/7 (41%) had difficulty in breathing and rapid bloating. The outbreak in both humans and animals occurred in Bunatsami subcounty and Nangako Town Council (Figure 3). Bunatsami sub-county was more affected (AR: 6 per 1,000) than Nangako town council (AR: 0.3 per 1,000) (Table 1).

Hypothesis generation findings: of the 21 case patients interviewed, 18 (86%) ate meat from an animal that died suddenly, 12 (57%) had participated in butchering (which included touching meat/body fluids, carrying sick animals, removing animal organs, touching skin/hides, slaughtering, skinning, presence of a wound at the

time of contact and doing soil related work); 10 (48%) cooked the meat. Based on the descriptive epidemiology and the hypothesis generation interview findings, we hypothesized that handling and eating meat from an animal that died suddenly was associated with an increased risk of anthrax infection.

Retrospective study findings: the villages where we conducted the cohort study had a total population of 441. However, we were only able to interview 216 persons who were present in the area at the time of the outbreak. Participating in butchering, preparing, and eating meat of an animal that died suddenly was associated with an increased risk of developing anthrax infection (Table 2). At the multivariate level (common group reference analysis), females were less likely to develop anthrax in comparison to men. People who did not cook but ate meat were 84 times more likely to develop anthrax in comparison to those who did not cook or eat; while people that cooked and ate meat were 122 times more likely to develop anthrax than those that did not cook or eat (Table 3).

Laboratory investigations: out of 30 human samples collected, six were confirmed, and all animal samples (4) tested were confirmed positive.

Environmental findings: both soil samples were confirmed positive. Due to the hilly nature of the affected area, animal owners practice zero grazing where they routinely obtain grass surrounding their homesteads and nearby river banks, for feeding their animals. The affected community lies beneath a hill and River Tsutsu. No human and animal cases were identified across the other side of the river.

Discussion

The 2022 anthrax outbreak in Bududa District marked the first confirmed instance in the district, affecting both humans (AR: 10/100,000, CFR: 5%) and animals (CFR: 100%). The outbreak was predominantly of the cutaneous form, and most cases were among males involved in livestock-related occupations. Handling and eating this meat significantly increased infection risk, with those cooking and eating it being more likely to contract anthrax. The environmental investigations supported our epidemiological findings.

The outbreak among humans occurred following reports of sudden animal deaths, with subsequent laboratory testing confirming anthrax in the animals. These findings are consistent with other outbreaks reported globally [15]. All cases reported in this outbreak were known to have had contact with animals or their products before symptom onset. Previous investigations of outbreaks in Uganda that have been done recently also found the association of anthrax to the handling of meat from animals that died suddenly [16]. Contact with animals included any form of participation in butchering. Butchering is a largely male-dominated role, which explains why males are typically the most affected sub-group during anthrax outbreaks [17], and why adults are more affected than children. Butchering anthrax-infected animals, combined with limited vaccination, facilitates further environmental contamination with *B. anthracis* spores, propagating the outbreak among both animals and humans [18].

The observed CFR of 5% among human cases falls within the documented range for untreated cases of cutaneous anthrax (5-20%), and is approximately 1% when treated (4). The CFR for untreated cases varies by the form of anthrax; approximately 25-60% for the GIT form, while the inhalational form is almost always fatal [4,19]. The CFR reported among animals in this outbreak highlights the acute and often fatal nature of anthrax infection in farm animals, consistent with documented patterns in anthrax outbreaks worldwide [20]. Published literature corroborates these findings, illustrating the higher susceptibility and mortality rates among animals compared to humans. Our findings underscore the importance of timely healthcare seeking to improve outcomes,

prompt diagnosis, enhanced veterinary surveillance, and preventive vaccination strategies to mitigate the impact of anthrax outbreaks in both human and animal populations.

This outbreak investigation identified the occurrence of both GIT and cutaneous forms of anthrax, but predominantly the latter. This aligns with what has been reported globally [16]; the cutaneous form of anthrax accounts for 95% of naturally occurring anthrax cases [20]. The presence of the GIT form reflects a prevalent practice in developing countries where consuming meat from animals that die suddenly is common [20] which was identified as a key risk factor in this outbreak. Surveillance of anthrax in humans and animals is challenging due to a lack of awareness and identification of cases. Some individuals may have experienced mild, non-specific signs and symptoms of anthrax and thus were likely missed during case-finding. This may have contributed to an underestimation of the scope of the outbreak. Additionally, we lacked data on animal/livestock population sizes to characterize the outbreak epidemiologically among animals. The retrospective design and reliance on self-reported data introduce potential biases, including selection and recall biases, which may have influenced the observed associations between exposures and anthrax infection. Findings may have limited generalizability to other settings, especially those with different socio-cultural contexts, healthcare infrastructure, and patterns of livestock management.

Conclusion

This outbreak was characterized by both cutaneous and GIT forms, and was associated with handling and eating meat from cattle that died suddenly. The spread to new districts highlights a need for widespread risk communication about anthrax, and consideration of broad vaccination of animals in this region. While comparisons with similar studies support some consistency in findings, variations in settings and methodologies underscore the need for context-specific interpretations.

Recommendations and actions: we recommended vaccination of animals in and around the affected villages, enhanced surveillance of animal populations, and further epidemiological studies to better understand the outbreak among animals. We lobbied for subsidized costs of vaccination of animals (down to 2,500/=) to motivate community members to vaccinate their animals. This was taken up, and a vaccination exercise was conducted in the affected sub-counties. We also recommended prophylaxis to exposed persons and consideration of routine vaccination against anthrax. We conducted health education and community sensitization on identifying and reporting sick animals, dangers of eating and handling meat of animals that have died suddenly, and proper disposal of carcasses. Results from this investigation were presented to the National Task Force and Bududa District leadership. The government of Uganda imposed a ban on the sale and movement of livestock in Bududa and neighboring districts.

Competing interests

The authors declare no competing interests.

Authors' contributions

Zainah Kabami: led the investigation team, conceptualization, design, analysis, drafting and review of the manuscript; Zainah Kabami, Brian Agaba, Helen Nelly Naiga, Robert Zavuga, and Fred Monje participated in the investigation and data collection; Brenda Nakafeero Simbwa, Joshua Kayiwa and Saudah Namubiru Kizito supported data analysis; Lilian Bulage, Richard Migisha, Daniel Kadobera, Fred Monje, Issa Makumbi and Alex Riolexus Ario reviewed the manuscript. All the authors have read and agreed to the final manuscript.

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Tables and figures

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Figure 3: map showing the distribution of human and animal cases during an anthrax outbreak in Bududa District, Eastern Uganda, February - May 2022

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Table 1: attack rates by sex, village, and sub-county during an anthrax outbreak in Bududa District, Eastern Uganda, February - May 2022				
Characteristic	**Frequency (N=21)**	**Percentage (%)**	**Population**	**Attack Rate/1,000**
Sex				
Male	16	76	5,115	3
Female	5	24	5,102	1
Bunatsami sub-county	19	90	3,263	6
Bumabala lower village	6	29	77	5
Bunalakala village	4	19	108	4
Bumalakala village	4	19	87	3
Bumabala upper village	4	19	71	3
Muririnyi village	1	5	98	1
Nangako Town Council	2	10	6,954	0.3
Bunamasongo village	1	5	79	1
Bunabunyu village	1	5	145	1

Table 2: risk factors of anthrax, Bududa District, Eastern Uganda, February - May 2022		
Exposure	**Risk ratios (RR)**	**95% CI**
Age category		
10 – 19 (reference)		
<10	0.3	0.0 - 2.2
20 – 30	1.7	0.3 - 8.4
31 – 40	1.6	0.4 - 6.4
≥ 41	0.8	0.2 - 2.6
Sex (female)	0.3	0.1 - 0.7
Participation in butchering, preparation/eating of meat		
Touched meat/body fluids of animal that died suddenly	15.3	7.7 - 30.4
Carried sick animal/one that died suddenly	9.3	4.4 - 19.4
The slaughtered animal that died suddenly	13.3	8.3 - 21.3
The skinned animal that died suddenly	12.6	8.0 - 19.9
Removed animal organs	14.1	8.7 - 23.0
Touched skin or hides	14.1	8.7 - 23.0
Did you have a wound/ cut at the time of contact	13.3	8.3 - 21.3
Found dead animal remains in the garden	12.0	7.7 - 18.6
Cooked meat of an animal that died suddenly	16.0	7.8 - 33.0
Ate meat from an animal that died suddenly	116.1	16.1 - 835.8

Table 3: factors associated with human Anthrax outbreak based on common group analysis, Bududa District, Eastern Uganda, February - May 2022		
Exposure	**Risk ratios (RR)**	**95% CI**
Age category		
10 – 19 (ref)		
<10	0.3	- 2.3
20 – 30	1.7	- 8.4
31 – 40	1.6	- 6.4
≥ 41	0.8	0.2 - 2.6
Sex		
Male (ref)		
Female	0.4	0.2 - 0.9
Education level		
Primary (ref) None	1.5	0.9 - 2.7
≥ Secondary	0.5	0.1 - 1.7
Cooking/eating meat		
Did not cook or eat (ref)		
Ate but did not cook	84.4	18.4 -388.0
Cooked and ate	122.5	34.3 - 437.9
Participated in butchering		
Did not butcher (ref)		
Butchered	1.4	0.9 - 2.6

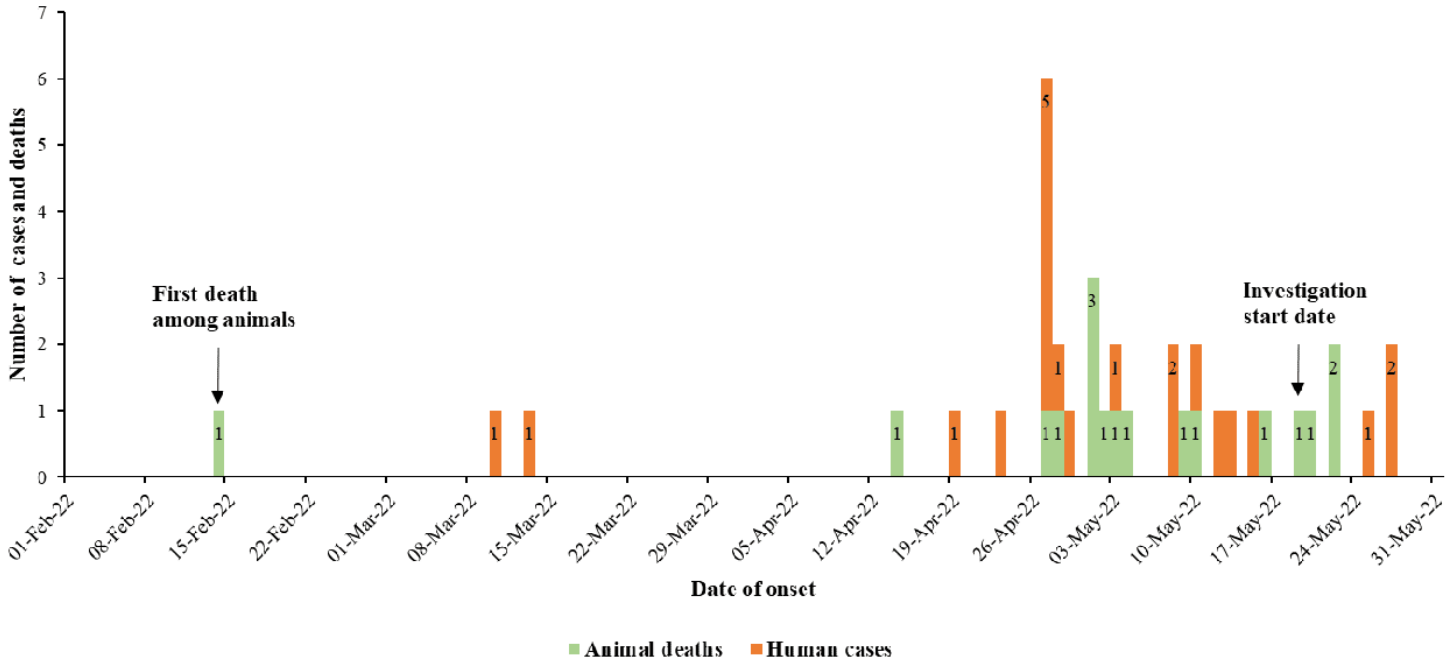

Figure 1: epidemic curve showing the distribution of case-patients and animal deaths, by onset during an anthrax outbreak, Bududa District, Eastern Uganda, February - May 2022

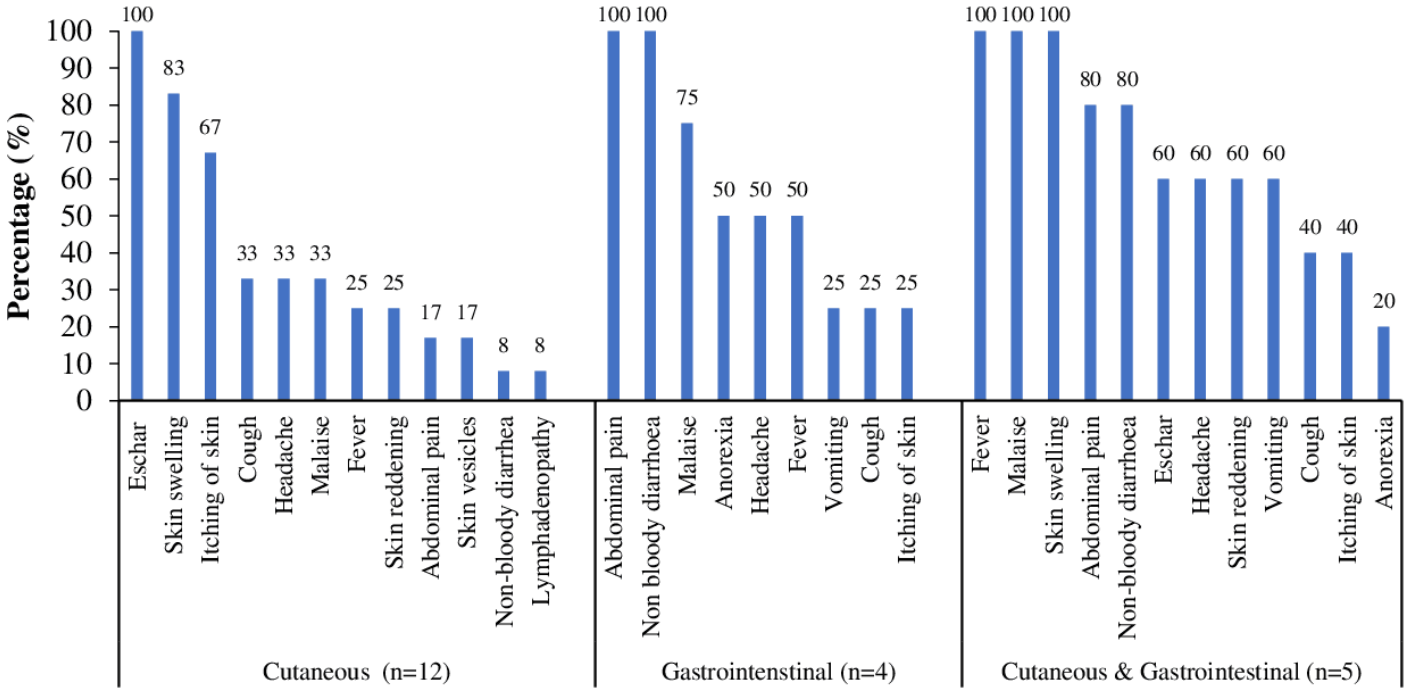

Figure 2: clinical manifestations of case patients during an anthrax outbreak in Bududa District, Eastern Uganda, February - May 2022

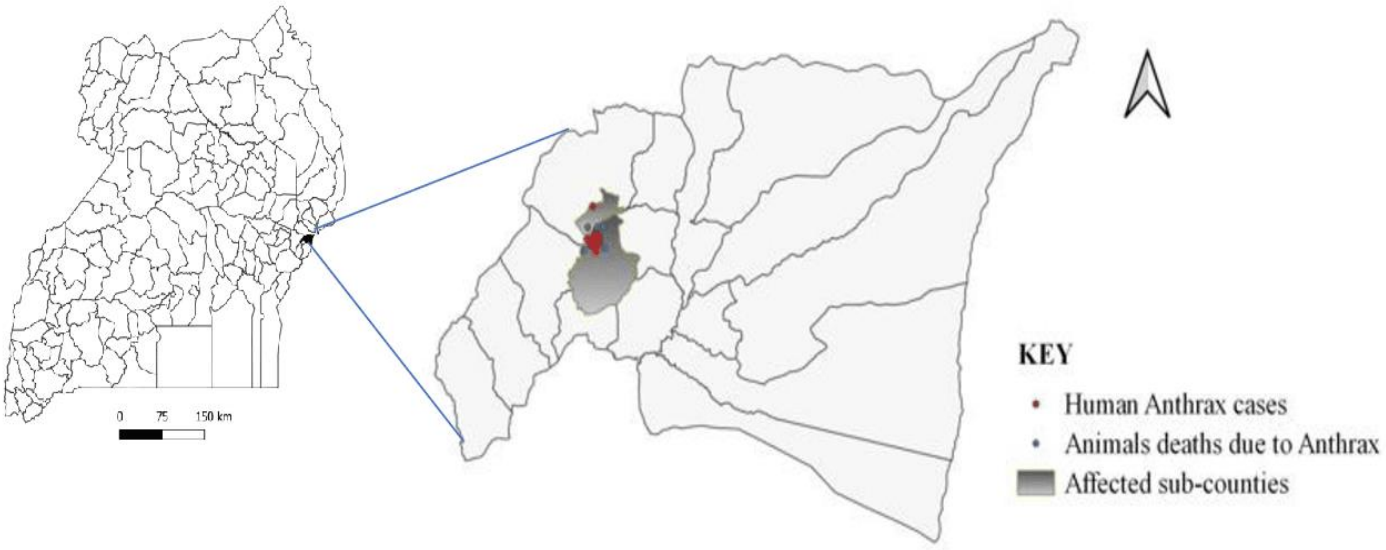

Figure 3: map showing the distribution of human and animal cases during an anthrax outbreak in Bududa District, Eastern Uganda, February - May 2022