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ORIGINAL RESEARCH ARTICLE

Health and Economic Burden of Rabies in Northwest Ethiopia

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Abstract

Background Rabies remains a significant threat to both public health and economic stability across many developing countries. The challenge of effectively managing and preventing rabies is compounded by insufficient quantitative data regarding its financial and health consequences. Despite Ethiopia being one of the most-affected countries in the world, data on the public health and economic burden of rabies are limited.

Objective This research aimed to quantify both the health and economic burden of rabies in northwest Ethiopia.

Method Follow-up and recording of potential rabies cases were conducted for 18 months in seven districts of northwest Ethiopia. Data were collected from potential rabies cases using a pre-planned checklist. The health and economic burden were quantified using deterministic models. The study primarily adopted a household/patient perspective, focusing on the direct financial burdens faced by individuals and families.

Results In the follow-up period, approximately 353 individuals were recorded as rabies victims. Among them, 126 households with suspected rabies cases were treated with traditional medicine, while 60 individuals from 59 households received post-exposure prophylaxis. The annual premature death rate due to rabies was estimated to be 3.14 per 100,000 population. The annual years of life lost due to premature death was estimated to be 90.69 per 100,000 population. Years lived with disability due to rabies illness, disability due to post-exposure vaccine, and traditional treatment were estimated to be 0.68 per 100,000 population. The annual health burden of rabies was estimated to be 91.34 disability-adjusted life years per 100,000 people. The total cost for rabies control measures in humans was estimated to be United States (US) $11,474.66. On average, each household spent US $40.55 on post-exposure prophylaxis, with an annual cost of US $27.03 per household. Regarding livestock, the losses due to rabies were estimated to be US $29,599.85 annually, which translates to an approximate loss of US $274.07 per household per year.

Conclusion The findings emphasise the need for targeted interventions to mitigate rabies' disproportionate impact on vulnerable communities, aligning with global efforts to eliminate the disease by 2030. A One Health approach that integrates rabies control in human and animal health is suggested.

Key Points for Decision Makers

Rabies is a cause of significant health burden in northwest Ethiopia.

Rabies causes significant economic burden in northwest Ethiopia.

Controlling rabies using a One Health approach is important in northwest Ethiopia.

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1 Introduction

Rabies is an ancient disease that has caused the death of thousands of people around the world from time immemorial and is still a major veterinary and public health problem [1]. It is a zoonotic viral disease caused by *Lyssavirus* from the *Rhabdoviridae* family. It affects all warm-blooded animals. Carnivores and bats are the major reservoirs of the virus. Domestic dogs are the main source of human exposure in most rabies-endemic countries of Africa and Asia [2] and have the greatest risk of contracting rabies anywhere in the world [3]. Rabies is one of the most fatal of all infectious diseases in humans and causes severe economic impacts in many developing countries [4]. In developing countries, 99% of human mortality from rabies is due to bites from rabid dogs. Human rabies, which originated from dogs, is endemic to the entire African continent, where cases are often highest in rural communities of resource-limited countries [5]. Rabies has been eliminated (or historically been absent) in Western Europe and several island nations such as Japan, Australia, and New Zealand [6].

In 2014, the Global Alliance for Rabies Control (GARC) started the Pan-African Rabies Control Network (PARACON), aiming to create a consolidated One Health network for rabies management throughout sub-Saharan Africa using available evidence to plan and support rabies prevention and control and eventual canine rabies elimination [7]. In 2015, the World Health Organization (WHO), the Food and Agriculture Organization, the World Organization of Animal Health, and the GARC set a global call for action against rabies. The goal was to achieve zero human deaths from dog-mediated rabies by 2030 [8]. These efforts need evidence-based information about the impacts of rabies.

Though no accurate data are available on the global burden of rabies, direct mortality due to the disease is estimated to be among the highest. The annual number of human rabies deaths globally is estimated to be 61,000, with the vast majority of deaths occurring in rural areas [8]. It was reported that rabies causes a loss of 3.7 million disability-adjusted life years (DALYs) per year and about United States (US) $8.6 billion of economic losses, mainly due to premature deaths (productivity losses) and post-exposure treatment (PET) costs [9]. The annual cost of rabies in Africa and Asia was estimated at US $583.5 million, most of which was due to the costs of PET [10].

Ethiopia is one of the worst-affected countries [8], with domestic dogs being the major source of the infection, associated with the huge dog population and ineffective dog management [11]. Although rabies has been known in Ethiopia for centuries in society as "mad dog disease" [3], its impact has remained unknown or underestimated. Rabies occurs with a high incidence in both humans and animals, which could be a significant public health and economic burden in the country. Approximately 10,000 people are estimated to die of rabies annually in Ethiopia [12]. A relatively recent study by Beyene et al. [13] reported an annual estimate of approximately 3000 human deaths, resulting in about 194,000 DALYs per year and, on average, US $2 million treatment costs per year. Because the majority of victims pass away at home, the disease is also badly underreported. As a result, public health agendas fail to give rabies prevention enough priority [9].

Control of rabies is impeded by a lack of information about its true consequences in many developing nations [14]. To be engaged in collaborative action against rabies, policy makers should be aware of the potential health and economic burden of rabies. There is a lack of accurate quantitative information on the public health and economic burden of rabies, both in the human health and veterinary sectors, in the Amhara region of northwest Ethiopia. Therefore, this study aimed to quantify the health and economic burden of potential rabies cases in northwest Ethiopia.

2 Materials and Methods

2.1 Descriptions of the Study Area

The current study was conducted in the northwest part of the Amhara region of Ethiopia. The Amhara region is divided into 11 zones and 167 districts with about 3429 kebeles [15]. The total population is estimated at around 22,877,365, of which about 88% is rural, while 12% are urban dwellers [16]. The current study was conducted in four zones of Gondar within the Amhara region. From these zones, seven districts were selected: East Dembia and Tach Armachiho from the Central Gondar zone, Genda Wuha and Metema from the West Gondar zone, Fogera and Debre Tabor from the South Gondar zone, and Debark from the North Gondar zone (Figure 1). The study area has a total estimated human population of 5,464,079 and a total livestock population of 5,474,545 cattle, 2,484,400 sheep, 2,461,942 goats, 44,860 horses, 847,780 donkeys, and 6609 dogs [16, 17].

2.2 Study Population

The study populations were humans, livestock, and dogs found in the study area. The human population was essential for assessing DALYs and the economic burden (cost of PET, accommodation, transportation, traditional medicine, etc.) related to rabies. Livestock data were collected to calculate productivity losses (time lost) and direct losses resulting

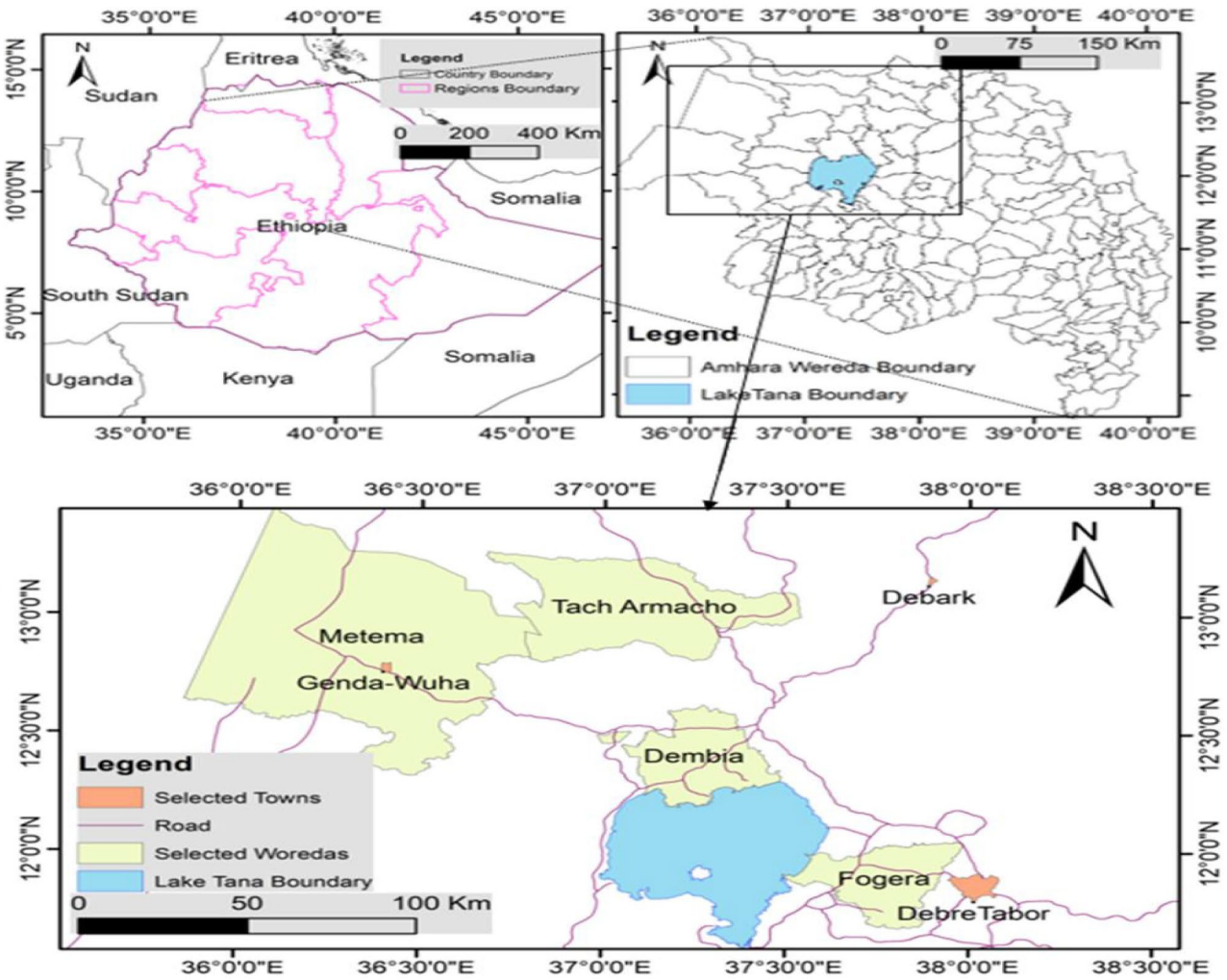


Fig. 1 Map of the study area

from the death of animals due to rabies. For dogs, data were gathered on vaccination costs as well as productivity losses incurred during the vaccination process (time lost).

2.3 Sampling Design

First, the four zones of Gondar were selected based on their ease of accessibility for the study. Two districts (the principal town and rural district, representing, respectively, the urban and rural parts of the zones) were selected purposefully. The study population in the selected districts was prospectively followed up for potential rabies cases, including rabies exposures (bitten by suspected, probable, or confirmed rabid animal as described by the WHO [8]), and rabies suspected cases (cases showing clinical signs of rabies but the history of exposure is not known). Upon the notification of potential rabies cases by the assigned animal health person, the study team mobilised to the area, and laboratory samples were collected for confirmatory diagnosis in the case of suspected animal cases and relevant data were collected using a pre-planned data collection checklist. A rabies outbreak occurred in the area before starting the data collection. In this way, the follow-up and data collection for the occurrence of potential rabies cases in all selected districts was done from 15 July 2022 to 15 January 2024 for 18 months.

2.4 Data Collection Checklist for Potential Rabies Cases

A checklist aiming to collect data required to estimate the health and economic burden of potential rabies cases was prepared (Supplementary file S1; see the electronic supplementary material). The checklist had two parts. The first part of the checklist included data on the demography of infected individuals and questions used to collect data

regarding biting dogs' behaviour and clinical manifestation at the time of them biting humans and/or animals. The second part included data related to the costs of post-exposure vaccination (PEV), wound care activity, and disinfection, costs of antibiotics, costs of transportation, costs of accommodation and food, and opportunity costs of time of the victim and their caretakers while seeking treatment following rabies exposure. Questions about adverse effects of treatment vaccination and death associated with rabies were also included in the second part of the checklist. Data about the number of animals affected, costs of animal treatment, animal owners' time spent regarding treatment, and the number of animals infected by or dead due to rabies were also recorded.

2.5 Estimation of Health and Economic Burden of Rabies

The health and economic burden of rabies was estimated based on the cost classification of Jo [18]. In this framework, direct costs include expenditures for post-exposure prophylaxis (PEP), traditional medicine, transportation, and accommodation covering both healthcare and non-healthcare expenses quantified in monetary terms. Indirect costs consist of losses in DALYs and opportunity costs of time lost by victims and caregivers while seeking treatment, losses due to livestock death or precautionary slaughter (minus salvage value), and productive loss due to premature death, as summarised in Table 1.

2.5.1 Estimation of the Health Burden of Rabies

The health burden of rabies was estimated in terms of DALYs. DALYs were calculated as the sum of years of life lost (YLL) due to premature mortality and years lived with disability (YLD) [19] associated with rabies illness, adverse effects of nerve-tissue vaccine (NTV), and adverse effects of traditional medicaments.

The YLL due to rabies was estimated from expected years of life lost at death derived from the standard life table for Ethiopia as given by the WHO [20] and from the number of deaths due to rabies as follows:

$$\mathrm{YLL}_i = \sum_{i=\mathrm{Birth}}^{n} (N_i^R * E_i) \quad (1)$$

where: YLL_i = years of life lost due to mortality of rabies in a household, N_i^R = number of human deaths due to rabies in the household with age category i, E_i = life expectancy of the concerned category of age i ($i = 0 \ldots 18$) in gender difference.

The YLD was calculated for disability caused by the illness due to the disease and adverse effects of vaccination and traditional treatments.

The YLD due to the rabies illness was calculated as follows:

$$\mathrm{YLD}_R = \mathrm{NV}_{i^R} * \mathrm{DD}_{i^R} * \mathrm{DW}^R \quad (2)$$

where:YLD_R= years lost due to disability associated with rabies itself in a household, NV_{i^R} = number of victims who are exposed to potentially rabid animals in a household, DD_{i^R}= duration of disability in days with rabies exposure in a household, DW^R= disability weight of rabies disease, i.e. 0.133 [21].

Disability due to adverse effects of NTV was calculated from the number of victims who got NTV, duration of vaccination, and disability weight of NTV, as shown in Eq. 3:

$$YLD_R = NV_{i^R} * DD_{i^R} * DW^R \quad (3)$$

where: YLD_{vi} = years lost due to disability associated with adverse effects of NTV in a household, NV_{vi} = number of victims who got NTV in a household, DD_v = duration of disability in days due to NTV in a household, DW^R disability weight of the NTV, i.e. 0.613 [10].

Disability due to adverse effects of traditional medication was calculated from the number of victims who were treated by traditional medication, duration of disability, and disability weight of complications due to traditional medication, as shown in Equation 4:

$$\mathrm{YLD}_{\mathrm{TM}i} = \mathrm{NV}_{\mathrm{TM}i} * \mathrm{DD}_{\mathrm{TM}i} * \mathrm{DW}_{\mathrm{TM}} \quad (4)$$

Table 1 Cost classification for burden of rabies exposure

Direct costs		Indirect costs
Health care costs	Non-healthcare costs	
Diagnosis	Transportation	Mortality (DALYs)
Vaccine (PEP)	Accommodation and food	Morbidity (DALYs)
Wound care and disinfection		Opportunity costs of time lost by victims and caregivers while seeking treatment
Antibiotics		Losses due to livestock death or precautionary slaughter (minus salvage value)
Traditional medicines		Productive loss due to premature death

DALY disability-adjusted life year, *PEP* post-exposure prophylaxis

where: YLD_{TMi} = years lost due to disability associated with traditional medication discomfort in a household, NV_{TMi} = number of victims who experienced traditional medication discomfort in a household, DD_{TMi} = duration of disability in days due to traditional medication side effects in a household, DW_{TM} = disability weight of traditional medication; the sum of 0.223 for a headache [21] and 0.247 for severe diarrhoea [22] was used for the disability weight of traditional medication, as headache and severe diarrhoea are common complications of traditional medicines in Ethiopia.

The DALYs (YLL + YLD) calculated for each household in the study were summed to calculate the health burden for the study population, and this burden was expressed per household and also per 100,000 population.

2.5.2 Estimation of Economic Burden of Rabies

Economic burden of human rabies The economic burden of human rabies was estimated from costs of diagnosis, costs of PET, cost of traditional medicine (when applied), and cost of seeking treatment, which includes the victims' and their caretakers' transport, accommodation, time, and cost of medicaments.

Costs of PET

$$C_i^{PEV} = NV_i^{PEV} * C^{PEV} \quad (5)$$

where: C_i^{PEV} = costs of PEV following rabies risk (exposure) in a household, NV_i^{PEV} = number of victims with risk of exposure in a household, C^{PEV} = costs of one complete PEV

Costs of time for caregivers and victims A complete course of NTV for PEV consists of 17 doses of vaccine administered consecutively for 14 days followed by booster doses for 3 days in 10-day intervals, i.e. at day 24, 34, and 44 [20]. Therefore, the time lost by caregivers and the victims includes these days/hours and the days/hours for transportation, depending on how far it was between their residence and the location of the clinic/hospital where the victim got vaccination service.

Costs of victims' time

$$C_i^{VT} = NV_i^{PEV} * TV_i^{PEV} * P_i^{LH} \quad (6)$$

where: C_i^{VT} = costs of victims' time for taking PEV in household, NV_i^{PEV} = number of victims with PEV due to risk of rabies in household, TV_i^{PEV} = time losses (in hours) of victims while taking PEV in household, P_i^{LH}= price of labour per hour (25 Ethiopian Birr) in Amhara region. We gathered such information from the interviewees directly during data collection; however, there is no previous information or published article about this price. Therefore, we use as the primary information

Costs of time of caregivers

$$C_i^{CGT} = N_i^{VPEV} * T_i^{IC} * P_i^{LH} \quad (7)$$

where: C_i^{CGT} = costs of caregivers' time to nurse a victim in the household, NV_i^{PEV} = number of victims with PEV due to risk of rabies in household, T_i^{CG} = time taken by caregivers (in hours) to nurse a victim in a household, P_i^{LH}= price of labour per hour (25 Ethiopian Birr) in Amhara region.

Costs of transportation and accommodation Cost of transportation and cost of accommodation can be multiplied by the number of persons who were bitten by a potentially rabid animal and travelled to find treatment with their accompanying caregivers.

$$CVC^{TA} = (NV^{T} * C^{TA}) + (N^{CG} * C^{TA}) \quad (8)$$

where:

CVC^{TA} = costs of victims' and their caregivers' transportation and accommodation in household

NV^{T} = number of bitten persons who travelled to find treatment in household

C^{TA} = cost of transportation and accommodation per person in household

N^{CG} = number of caregivers accompanying the bitten victims in household.

Cost of traditional medicine Costs related to traditional medicine treatment were calculated as follows:

$$CTM = NVTM * CTMP \quad (9)$$

where: C^{TM} = total cost of traditional medicine in household, NV^{TM} = number of victims taking traditional medicine in household, C^{TMP} = cost for traditional medicine per person in a household.

Overall cost of human rabies control The overall cost of human rabies control is calculated as follows:

$$TC_{RH} = C^{PEV} + C^{VT} + C^{TM} + C^{CGT} + CVC^{TA} \quad (10)$$

where: TC_{RH}= total cost of rabies control in human, C^{PEV} = costs of PEV following rabies risk (exposure) in a household, C^{TM} = total cost of traditional medicine in household, CVC^{TA} = costs of victims' and their caregivers' transportation and accommodation in household, C^{VT} = costs of victims' time for taking PEV in household, C^{CGT} = costs of caregivers in household.

2.5.3 Estimation of Economic Burden Associated with Livestock Rabies

The economic burden of rabies associated with livestock was estimated based on the mortality of livestock due to rabies, livestock that were slaughtered as a precautionary measure as owners did not want to face the risk that their cattle might gradually develop clinical signs (they slaughter the animals and sell the meat to their neighbours), and the costs

of treatment or preventive measures, including the opportunity cost of the owner's labour spent seeking treatment or prevention measures. The study primarily adopted a household/patient perspective, focusing on the direct financial burdens faced by individuals and families. This approach captured out-of-pocket medical expenses (e.g. treatments, medications) and lost income due to illness or caregiving responsibilities, reflecting real-world economic impacts on households. While rooted in individual-level costs, the analysis partially incorporated societal considerations by including indirect costs such as lost productivity/time and livestock losses.

Costs due to mortality of livestock Costs due to mortality of livestock were estimated as follows:

$$\mathrm{CMS}_{ij} = N_{ij} * \mathrm{AvP}_{ij} \tag{11}$$

where: CMS_{ij} = costs of livestock due to mortality in species of animal i and age category j, N_{ij}= number of livestock dead due to rabies in species of animal i and age category j, AvP_{ij} = average price of livestock dead or slaughtered due to rabies in species of animal i and age category j.

Costs of slaughter as a precautionary measure due to suspected rabid dog bite The costs of livestock slaughter as a precautionary measure due to a suspected rabid dog bite were estimated as follows:

$$\mathrm{CC}_{ij} = \mathrm{NC}_{ij}(\mathrm{AvP}_{ij} - \mathrm{AVSP}_{ij}) \tag{12}$$

where: CC_{ij} = costs of culling livestock due to suspected rabid dog bite in species of animal i and age category j

NC_{ij} = number of livestock culled due to suspected rabid dog bite in species of animal i and age category j

AvP_{ij} = average price of livestock culled due to suspected rabid dog bite in species of animal i and age category j

AVSP_{ij}= average salvage value of livestock culled due to suspected rabid dog bite in species of animal i and age category j.

Costs of treatment or preventive measures for an animal with suspected rabid dog bite The costs of treatment or preventive measures for an animal with a suspected rabid dog bite were estimated as follows:

$$\mathrm{CTP}_{ij} = N_{ij} * \mathrm{AvCTPM}_{ij} \tag{13}$$

where: CTP_{ij} = costs of treatment or preventive measures for an animal due to a suspected rabid dog bite in species of animal i and age category j, N_{ij}= number of treatments or preventive measures applied due to a suspected rabid dog bite in species of animal i and age category j, AvCTPM_{ij}= average costs of treatment or preventive measures applied due to suspected rabid dog bite in species of animal i and age category j.

Opportunity costs for labour spent seeking treatment or prevention measures for an animal The opportunity costs for labour spent seeking treatment or prevention measures for an animal were estimated as follows:

$$C_{\mathrm{FL}} = T_F * NP * P_{\mathrm{FT}} \tag{14}$$

where: C_{FL} = costs of farmer's labour spent seeking treatment or prevention measures for an animal due to a suspected rabid dog bite, T_F = time spent seeking treatment/preventive measures for an animal related to a suspected rabid dog bite, N_p = number of people (> 15 years of age) who went with the animal with the suspected rabid dog bite, P_{FT}= price of labour per duration of farmer's time spent for treatment or preventive measures applied due to suspected rabid dog bite of the animal.

Total economic burden associated with livestock rabies The total economic burden of rabies was the sum of the total costs due to livestock mortality or slaughter of livestock as a precautionary measure, the costs of culling livestock due to a suspected rabid dog bite, and opportunity costs for labour spent seeking treatment or prevention measures for an animal.

$$\mathrm{TEB}^{\mathrm{Rexp}} = \mathrm{CM}_{ij} + \mathrm{CC}_{ij} + \mathrm{CTP}_{ij} + C_{\mathrm{FL}} \tag{15}$$

where: $\mathrm{TEB}^{\mathrm{Rexp}}$ = total economic burden (loss) of rabies exposure in livestock in the study area within 18 months of data

CM_{ij} = costs due to livestock mortality in species of animal i and age category j, CC_{ij} = costs of livestock slaughtering as a precautionary measure due to suspected rabid dog bites in species of animal i and age category j, CTP_{ij} = costs of treatment or preventive measures for an animal due to a suspected rabid dog bite in species of animal i and age category j, C_{FL} = costs of farmer's labour spent seeking treatment or prevention measures for animals due to a suspected rabid dog bite.

2.6 Sensitivity Analysis

To ensure the robustness and reliability of our estimates for both the health and economic burden of rabies, we conducted two complementary types of sensitivity analyses: one-way sensitivity analysis and probabilistic sensitivity analysis.

One-way analysis tested individual parameters (vaccine costs, labour costs, livestock values, exchange rates) while keeping others fixed, revealing key cost drivers like labour and livestock expenses. For cost calculations, we used an average exchange rate of US $1 to 53.71 Ethiopian Birr. Given that only 1 month of 2024 was included in the study, the exchange rate for 2024 had minimal (no change) impact on our overall analysis. (We use as the reference the following website: https://www.exchangerates.org.uk/USD-ETB-spot-exchange-rates-history-2022 and 2023.)

Probabilistic analysis used bootstrap resampling to simultaneously vary uncertain parameters (bite incidence, PEP uptake, treatment costs), generating prediction intervals to quantify overall uncertainty.

Combining both methods strengthened the model's credibility: one-way analysis identified priority parameters for policy makers, while probabilistic analysis assessed cumulative uncertainty, ensuring robustness of the model. We conclude that the model demonstrated stability and reliability in current estimates after these evaluations.

2.7 Data Management and Analysis

All the data collected from victims and respondents about public health and the economic burden of rabies were entered into Excel. The data were checked for their completeness and consistency, and incomplete and inconsistent data were corrected where possible and removed otherwise. The descriptive statistics extensively used to summarise were the mean, minimum, maximum, and sum of the outcome of interest. The health and economic burdens were calculated using the deterministic models listed in Sect. 2.5, "Estimation of Health and Economic Burden of Rabies", using Eqs. 1–15.

3 Results

In the 18-month follow-up (15 July 2022 to 15 January 2024), approximately 353 individuals from 126 households with suspected rabies were treated using traditional medicine, 60 individuals from 59 households received PEP, while 20 cases did not undergo any treatment. Among these reported potential rabies cases, 27 humans and 208 animals died. The annual incidence of rabies mortality in humans was 3.14 per 100,000 population.

3.1 Summary of the Health and Economic Parameters

The health and economic impact estimates were based on the current outbreak and the control measures implemented by the communities. During this outbreak, farmers experienced losses ranging from a minimum of US $38.18 to a maximum of US $4047.35 due to culling and precautionary slaughter of livestock to prevent the spread of the disease. In addition to livestock losses, affected individuals incurred a maximum cost of US $385.64 for PEP as a control measure. The minimum, average, and maximum values of the key input items used for estimating the health and economic impact are summarised in Table 2

3.2 Estimation of Health and Economic Burden of Rabies

3.2.1 Health Burden of Rabies

The average annual health burden of rabies due to premature mortality in the study population was estimated at 90.69 YLL per 100,000 population in the current study. The annual health burden in the affected (case) households was 4.22 YLL per household (Table 3). The estimated health burden from NTV adverse effects was 0.33 DALYs per 100,000 population annually, while traditional medicine side effects

Table 2 Summary of the lowest, average, and highest values of the parameters applied in calculating the health and economic burden of rabies disease

Model parameters	Minimum	Average	Maximum
Number of exposed members in the household	1	3	9
Age of the victims (years)	1	29.04	80
Time spent to start PEP (days)	1	11.98	60
Time spent to complete PEP (days)	17	39.11	90
Cost of PEP per victim (USD)	0.19	56.66	385.64
Cost of caregivers losing productivity (USD)	0.02	0.13	0.31
Cost of victims losing productivity (USD)	0.12	0.34	0.94
Cost of transportation and accommodation (USD)	1.53	68.55	305.46
Cost of traditional medicine (USD)	0.21	360.68	2352.11
Costs of losing livestock in the household due to death (USD)	22.91	186.91	744.56
Costs of losing livestock in the household due to culling and precautionary slaughter (USD)	38.18	479.92	4047.35
Cost expended by farmers for treating animal due to rabies (USD)	0.52	7.17	68.73
Cost to farmers of losing productivity when they treated their animals (USD)	1.4	4.7	14.32

PEP post-exposure prophylaxis, *USD* United States dollars

Table 3 Estimation of premature death due to potential rabies exposure in individuals and per household

Individual victim ID	YLL
FID6	71.79
MID11	61.20
MID14	61.20
FID17	23.35
FID30	45.23
MID44	29.23
MID45	25.05
MID50	61.20
MID64	11.15
MID65	29.23
MID71	33.56
MID73	65.82
FID83	23.35
FID89	71.79
MID91	56.50
MID129	33.56
MID136	17.44
FID137	71.79
MID148	33.56
FID153	40.61
FID154	31.72
FID157	54.65
MID168	25.05
MID169	51.86
MID177	25.05
FID183	49.91
MID185	65.82
Total YLL	1171
Average YLL in 100,000 population/year	90.69
Average YLL in the affected household/year	4.22

ID identification number, *YLL* years of life lost

contributed 0.32 DALYs per 100,000. The total rabies burden (from YLL and YLD) was 91.38 DALYs per 100,000 people, with 99.22% attributable to premature rabies deaths and 0.78% to medication side effects (NTV and traditional treatments) and rabies disability time (Table. 4).

3.2.2 Economic Burden of Human Rabies

The total annual cost of human rabies control was estimated at US $11,474.66 in the study districts. The annual average cost of rabies control was estimated at US $41.35 per household in the current study districts. The average annual cost of transportation and accommodation for potential rabies cases seeking PEP was estimated at US $108.22 per household, which was the major contributor to the cost, followed by the cost of PET itself (US $27.03) per household of the affected case. The smallest contributor was the cost of time for caregivers (US $0.32). The average time of seeking PEP treatment was 11.98 (1–60) days, while the average time to finish treatment was 39.12 (17–90) days. The cost of traditional medicine for controlling rabies in humans was estimated to be US $23.72 per household in the current study (Table 5).

3.2.3 Estimations of the Economic Burden of Rabies in Livestock

During the study period, over 170 animals, including bovine, equine, caprine, and ovine species, from 108 households were bitten by animals suspected of rabies. The total economic losses, which include direct mortality from rabies and indirect costs such as time lost and labour expenses incurred by farmers seeking treatment or preventive measures for their animals, amounted to an estimated US $29,599.85 annually across these households. Among these costs, the highest was the expense for slaughtering animals as a precautionary measure following suspected rabid dog bites, totalling US $209.76. On average, each household lost US $61.18 due to direct animal deaths. Additionally, farmers experienced an average productivity loss of US $2.24 per household due to the time devoted to treating their animals. Overall, the annual economic loss caused by rabies was estimated at US $274.07 per household. The results are summarised in Table 6.

Table 4 Annual health burden due to rabies death, adverse effects of nerve-tissue vaccine (NTV), rabies disability, and traditional medicine

Variables	Debark	ED	DT	Fogera	GW	Metema	TA	Annually/100,000
YLL	263	255	0	152	0	156.4	344.67	**90.69**
YLD^{R}	0.01	0.13	0.05	0.08	0.031	0.055	0.05	**0.031**
YLD^{NTV}	0.15	1.33	0.29	0.74	0.74	0.596	0.45	**0.33**
YLD^{TRD}	0.67	1.29	0.27	0.57	0.12	0.598	0.66	**0.32**
DALYs	264	258	0.62	153	0.889	157.61	345.83	**91.34**

DALY disability-adjusted life year, *DT* Debre Tabor, *ED* East Dembia, *GW* Genda Wuha, *TA* Tach Armachiho, YLD^{NTV} years lost due to disability associated with NTV, YLD^{R} years lost due to disability associated with rabies itself, YLD^{TRD} years lost due to disability associated with traditional medicine, *YLL* years of life lost

Table 5 Annual cost of rabies control in USD per household in study area

Cost factors	Debark	East Dembia	Debre Tabor	Fogera	Genda Wuha	Metema	Tach Armachiho	Annual average HH cost
Rabies control costs	**1579**	**5242**	**314**	**1052**	**533.3**	**2056.3**	**701.2**	**160.31**
Costs of PEP	53.5	1241	53.07	358	121	281	285	27.03
Costs of time of caregivers	0.44	2.56	0.42	0.44	0.86	0.59	0.39	0.32
Costs of time of victims	0.64	4.13	2.07	1.97	1.4	2.71	0.85	1.02
Costs of transportation and accommodation	504	1751	128.7	509	248	844	236	108.22
Cost of traditional medicine	1020	2243	129.5	182	162	928.	179	23.72

HH household, *PEP* post-exposure prophylaxis, *USD* United States dollars

Table 6 Cost of livestock loss (dead, slaughtered, or culled) due to rabies and cost of control measures per household per year in USD

	Debre Tabor	Debark	East Dembia	Fogera	Genda Wuha	Metema	Tach Armachiho	Cost/HH/year
CM	0.00	5355.1	2210.8	114.6	0.00	1779.3	452.5	61.18
CS	286.37	2386.41	9688.8	2043	7312	6660.9	5603.28	209.76
CTP	0.00	5.38	0.00	0.00	68.7	64.66	4.677	0.89
C_{FL}	0.00	35.92	61.05	89.73	1.43	138.89	36.27	2.24
TEB	286.37	7782.81	11961	2247	7382	8643.75	6096.73	**274.07**

CM costs of livestock due to rabies mortality in species of animal, *CS* costs of slaughter as a precautionary measure due to suspected rabid dog bite in species, *CTP* costs of treatment or preventive measures for animal due to suspected rabid dog bite in species of animal, C_{FL} costs of farmer's labour spent seeking treatment or preventive measures for animal due to suspected rabid dog bite, *HH* household, *TEB* total economic burden (loss) by rabies exposure in livestock in the study area within 18 months of data, *USD* United States dollars

3.3 Sensitivity Analysis

One-way sensitivity analysis revealed that labour costs and livestock values play a significant role in driving the economic burden. This means that by targeting interventions in these areas, there is strong potential to significantly lower overall costs. While increases in labour costs and livestock prices introduced uncertainty into the estimates, fluctuations in the exchange rate had no impact on the level of uncertainty.

Probabilistic sensitivity analysis, using bootstrap resampling to simultaneously account for uncertainties in factors like bite incidence, PEP uptake, and treatment costs, provided prediction intervals that reflected the overall level of uncertainty. This uncertainty was lessened by directly confirming bite incidence and PEP uptake with patients. Still, rising treatment costs introduced some uncertainty, whereas fluctuations in the exchange rate did not impact the final results.

Both analyses confirmed that our estimates of the disease burden hold up well, even when we account for reasonable changes in key assumptions. This strengthens our main conclusion that rabies has a serious health and economic impact in northwest Ethiopia. As a result, the study's recommendations for focused and coordinated rabies control efforts are well backed by these findings.

4 Discussion

The present study confirms that rabies remains a serious public health and economic problem in developing countries in Africa where canine rabies is endemic, like Ethiopia. Apart from the health burden, bites from potentially rabid animals impose a substantial financial burden on affected households, especially for rural bite victims, who suffer excessively high costs of obtaining PEP compared to those from urban areas. The results presented in Table 5 show that the rural districts (Metema, East Dembia, and Tach Armachiho) incur higher transportation and accommodation costs compared to the town districts (Debre Tabor, Debark, and Genda Wuha). The annual rabid suspected animal bite exposure rate of humans was 33.53 per 100,000 population, and the annual rabies mortality rate in humans was 3.14 per 100,000 population, respectively, in the present study. This result is almost similar to that of a study conducted on the rabies burden in Côte d'Ivoire [23]. Abdulmoghni et al. [24] also reported that the annual mortality rate was 2 per 100,000 people in a study investigating the incidence, trends, and mortality of human exposure to rabies in Yemen, 2011–2017. However, our estimates on the number of exposures and deaths were a little higher than previous national estimates [25], consisting of

12 exposure cases per 100,000 inhabitants and 1.6 rabies deaths per 100,000 inhabitants, respectively. These differences might be due to the underreporting of the recorded data, while the current study was based on active longitudinal follow-up of the disease incidence. Data taken from a record book or hospital report usually underestimate the burden of the disease because most of the rural victims did not report to the health centre; instead, they would treat themselves, using traditional healers (medicaments) [13, 26]. Our result on the potential rabies case rate was almost similar to the previous study conducted in Ethiopia, which ranged from 19 to 137 per 100,000 inhabitants, stated by Beyene et al. [13].

The average annual health burden of rabies in the study population was estimated at 90.69 YLL per 100,000 population of the study districts (Table 3). The result indicated the disease continued as an important cause of mortality. The result is in agreement with a previous report by Deribe et al. [27], who stated that rabies did not decline in the number of recorded human cases over 20 years in Ethiopia. Although rabies is not comparable with other priorities (human immunodeficiency virus [HIV], tuberculosis [TB], and other communicable diseases) that cause a very high health and economic burden, our findings demonstrated that rabies causes significant health and economic hardship with a high likelihood of fatality for exposed inhabitants, calling for national attention. However, this figure showed that it is comparable with other national and global prioritised diseases [28]. The rabies YLL found in this study is higher than the mortality burden of most of the national and global prioritised diseases in Ethiopia from 1990 to 2015 as determined by the Global Burden of Disease Study 2015.

In the current study, the annual health burden was calculated to be 91.38 DALYs per 100,000 people. This is comparable with the results of a recent global rabies burden study [8], which reported Ethiopia suffered the highest national health impact due to rabies among the Southern African Development Community, with 86.4 DALYs per 100,000 inhabitants, or 73,390 DALYs nationally. Our current study did not consider the temporary disability related to the time lived with a severe open wound DALYs [29, 30]. The premature death from rabies or YLL was the primary cause of this health burden, contributing to 99.22% of the rabies DALYs. The estimated health burden resulting from NTV treatments was 0.33 DALYs per 100,000 population annually. Less than 1% of the total DALYs was contributed by the side effects of medication (NTV therapy) and the disabilities of rabies illness. Similarly, previous studies reported that the health burden due to the adverse effects of NTV was 1% of the total rabies health burden [9, 13, 23]. This indicated that the communities still have a low awareness of NTV usage or the low income of the community, especially rural ones. The result showed that most of the victims went to traditional healers rather than modern health centres because of the lesser payment. As shown in Table 5, the annual average payment for traditional medicine was US $23.72 per house hold, while the amount for modern health centres was US $27.03.

The annual cost of human rabies control was estimated at US $7651.03 per 288 victims in the study districts. The annual average cost of rabies control was estimated at US $41.35 per household of the affected (case) in the study districts. The average annual cost of transportation and accommodation for potential rabies cases seeking PEP was estimated at US $108.22 per household, which was the major contributor to the cost, followed by the cost of PET itself (US $27.03) per household of the affected case. The smallest contributor was the cost of time for caregivers (US $0.32). The cost of traditional medicine for controlling rabies in humans was estimated at US $23.72 per household in the current study (Table 5). These estimations included direct healthcare, non-healthcare costs, and indirect costs of all potential rabies cases, which account for all types of treatment received (modern and traditional). Generally, non-healthcare costs account for the largest part of total PET costs. The non-healthcare costs per sufficient treatment were higher in each district relative to the PET cost because the PET centres (Gondar and Bahir Dar Hospital) were found far from the study districts. The largest portion of non-healthcare costs in distant districts like East Dembia and Metema (distant from the treatment health centre and rural districts) are because of transportation and accommodation payments.

Concerning seeking PEP and finishing a sufficient dose of PET, the average number of days spent was 11.98 (1–60) days and 39.12 (17–90) days, respectively. This might be due to the health centre's inaccessibility in terms of distance for the majority of the rural districts, as the Gondar Health Centre and Bahir Dar Addis Alem Hospital are the only facilities providing PEP [26]. On the other hand, victims who spend more time with disabilities might lack awareness about the facility for rabies disease because health extension workers and other respective organs give attention to funding-receiving diseases like HIV, malaria, TB, and so on. Our result was supported by the previous report by Beyene et al. [13], who stated that in Ethiopia, priority has been given to diseases like malaria, HIV/acquired immune deficiency syndrome (AIDS), and TB, and rabies gets low attention [31]. The number of days spent by potential human rabies cases to finish a sufficient dose of PEP treatment ranged from 17 to 90 days per case. The same scenario happened for getting sufficient PEP treatment in the previous study in Ethiopia [13]. A lack of awareness of the magnitude of the rabies problem and a lack of real data on epidemiological trends might hinder control initiatives conducted by policy makers as well as governments [32]. Because of that, the community health workers give less attention to the follow-up of rabies patients.

The annual overall cost for rabies control in humans was estimated at US $160.31 per household of the victims in the current study. The result indicated that rabies exposure continues to be not only a cause of human premature mortality but also has a significant economic impact on households when a member is potentially exposed to rabies. As the WHO [33] reported, managing a rabies exposure, where the average cost of rabies PEP is currently estimated at an average of US $108 (along with travel costs and loss of income), can be a catastrophic financial burden on affected families whose average daily income may be as low as US $1–2 per person. Hence, findings showed the costs related to rabies prevention and control measures in the study area were greater than the world average estimation.

For this deterministic analysis, the result is composed of two parts: loss of livestock due to rabies and the prevention of rabies in livestock. During the study period, 170 animals (bovine, equine, caprine, and ovine) from 108 households were bitten by potentially rabid suspected animals. The annual economic losses resulting from rabies exposure were from livestock loss and the indirect cost due to time lost and the costs of farmers' labour spent on seeking treatment or prevention measures for bitten animals. The direct and indirect cost was estimated at US $274.07 per household of the victims of the study districts. Out of this, US $61.18 was due to mortality and US $3.13 was due to indirect costs. According to a previous study on livestock-derived income, the average annual income from livestock per household in Ethiopia was estimated to be around US$300-$500 [34]. The current estimate of rabies livestock cost for potential case households is greater than the annual average income derived from livestock, which means rabies has a serious economic impact in exposed households. Similar results were reported in different regions of Turkey [35]. Hence, according to the results of the current study, rabies causes an economic crisis by affecting over half of the annual income per household in Ethiopia [16].

4.1 Limitations of the Current Study

The study demonstrates that rabies imposes a considerable health and economic burden in northwest Ethiopia, particularly affecting vulnerable rural populations, and calls for integrated, targeted interventions to control and eventually eliminate rabies. Despite our best efforts to actively track rabies cases, it is likely that some cases were missed, especially those where people died at home or sought help outside formal healthcare systems. Our methodology focused on active follow-ups of the disease, but we focused mainly on districts that were easier to reach. This means some cases, especially from harder-to-access places, might have slipped through the cracks. Because we did not select sites randomly, our findings might not apply equally across the entire region. We also relied a lot on self-reported information from individuals and households, especially when estimating the costs related to rabies. This can introduce some bias or inaccuracies, since people might not remember everything perfectly.

Livestock losses might be underestimated too, since not all are reported, particularly in communities where animals graze together in remote areas. As a result, the data and conclusions may not fully reflect the actual situation across all affected communities, making it harder for policy makers to accurately prioritise resources and interventions based on these findings. The current study also has limited generalisability due to its focus on a specific localised area. Additionally, the cost analysis was confined to expenses incurred at the household level, excluding fixed costs such as professional salaries, surveillance expenses, and similar overhead costs (fuel cost per-dim cost of the health and professional costs, etc.).

5 Conclusion and Recommendations

In conclusion, this study provided important information about potential rabies cases and the burden on the health and economy of the communities in the northwest part of Ethiopia. The disease continues to threaten the health and economy of the community and the county. Rabies causes the loss of income and productivity resulting from the illness or death of a family member, which can further exacerbate the burden on households. Therefore, rabies needs more attention from national and global health workers as well as policy makers. The findings emphasise the need for targeted interventions to mitigate rabies' impact on vulnerable communities, aligning with global efforts to eliminate the disease by 2030. A One Health approach that integrates rabies control in human and animal health is suggested.

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Data availability Human and animal data we use for health burden and economic losses.

Declarations

Ethical Approval and Consent to Participate This study was performed in line with the principles of the Declaration of Helsinki, and approval was granted by the Institutional Ethical Review Board (IERB) of the University of Gondar. The study protocol and consent procedure were approved by the IERB of the University of Gondar; the research project entitled "Epidemiology, Public Health and Economic Burden of Rabies in North-West Ethiopia" has been reviewed by the

IERB of the University of Gondar for its ethical soundness, and it is found to be ethically acceptable. Thus, the Research and Technology Transfer Vic President Office has awarded this ethical clearance for the study, as mentioned above, to be reported by Mr. Workneh Wondimagegn as the Principal Investigator and Dr. Sefinew Alemu and Professor Wudu Temesgen as co-investigators, as of July 8, 2022 (ref. no. VP/RTT/05/1037/2022, July 27, 2022). All the respondents were approached verbally and agreed to participate in the interview without any payment. The requirement for participant consent for publication of study results was waived by the IERB of the University of Gondar, and the study participants were kept anonymous to maintain their medical confidentiality rights. Data were analysed and reported anonymously.

Data Sharing Statement The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request. No custom code was generated or used for this study. All analyses were performed using Excel 16 version.

Conflict of Interest The authors report no conflicts of interest in this work.

Author Contributions All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; they took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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