Original Research Article

Economic Burden of Rabies: An experience from a tertiary care hospital in Kashmir, India

Comment [MC1]: I suggest the heading to be like this but you can modify it if you are not happy with it. In the earlier version, the sub-title was a repeatition of the title, which did not make much sense
Alright ,continue with the same title

Abstract:

Background: Post exposure prophylaxis (PEP) is the mainstay of prevention in suspected exposure to rabies virus. Exposed patients are able to obtain anti-rabies vaccine in the anti-rabies clinic pro bono but they have to pay for passive immunization and cover other associated costs.
Aim: To estimate and analyze the direct and indirect costs of rabies post-exposure prophylaxis.
Methods: This study was conducted on 429 patients, who were exposed to bites from various animals and reported to the tertiary healthcare centre,Shri Mahraja Hari Singh Hospital(SMHS) an associated hospital of Government Medical College, Srinagar, Kashmir. Patient socio-demographic profile, details of animal bite exposure, the cost incurred for PEP were collected. The data were analyzed using a descriptive statistic.
Results: The study revealed a total median cost incurred on patients for receiving a PEP as 29.3 USD(United States Dollar), with an Inter-quartile Range (IQR) of 0.2 USD to 43.1USD.The direct median cost was 20.5 USD with an IQR of 6.2 USD to 29.4USD, while the indirect median cost was 20.3USD with an IQR of 13.5USD to 24.4USD.
Conclusion: Post-exposure prophylaxis imposes a significant economic burden to bite victims especially those of low socio-economic strata for whom the cost is substantial.

Key words:- Post-exposure prophylaxis, Rabies immunoglobulin(RIg).Equine rabies immunoglobulin(eRIg)

Background:

Rabies an important viral zoonoses, owing to its high incidence, human and veterinary costs, and mortality, imposes tremendous burden annually in various countries[1, 2].Despite being a preventable disease through vaccination, tens of thousands of deaths occur annually worldwide. Across Asia, the annual expenditure secondary to rabies is estimated to be

staggering 563 million USD [3] .In India, 25 million USD are spent annually on post-exposure prophylaxis (PEP) [4,5]. The average spending on PEP is 49 USD in Asia where the average daily income is 1-2 USD per person, which imposes catastrophic financial burden on the affected families. [6]. The disability-adjusted life year (DALYs) associated with *Rabies* exposure is estimated to be 32,000 DALYs in Africa and 140,000 DALYs in Asia [7].Apart from the cost, the psychological impact after a suspected rabid dog bite cannot be translated into monetary value.

The biggest challenges in rabies elimination in low and middle-income countries (LMICs)are the stray dog populations, limited veterinary and human health infrastructure, low disease awareness and absence of efficient communication between the veterinary and the human health sectors. The lack of efficient control over growing stray dog populations is proving exceedingly costly in terms of DALYs lost as well as the cost of PEP to the public and private health sectors [8-10] The highest cost mainly accrues from rabies immunoglobulin (RIg), which, according to World Health Organization (WHO) guidelines must be injected on day zero together with a first active vaccination dose for category III exposure[7]. The WHO rabies exposure categories are, category I, touching or feeding animals, animal licks on intact skin (no exposure), category II, nibbling of uncovered skin, minor scratches or abrasions without bleeding (exposure),category III, single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (severe exposure).

Although India has made a lot of efforts to tackle mortality and morbidity associated with rabies, elimination of this disease remains a dream and the risk of contracting rabies has not changed much despite the provision of PEP, which may even have increased owing to the growing canine population. [7]. In view of the goal of elimination of dog-mediated human rabies by 2030 [11], jointly outlined by the WHO, Food and Agriculture Organization (FAO), and the Global Alliance for Rabies Control, there is a pressing need to have robust data on the socio-economic burden of rabies where dog bites wreak havoc. Our study sought to analyze and measure costs of the PEP in Kashmir.

The hospital has a separate Anti-rabies clinic which was among few such in India which implemented the Intradermal regimen based on the modified Thai Red Cross four dose Regimen (2-2-0-2-2) in 2011, and this practice is followed in most Asian countries.

The daily turnover of patients receiving PEP for rabies in the clinic is c.70-80 (old and new cases). We follow the WHO-recommended protocol for PEP, which includes prompt wound toilet, Anti-Rabies vaccine (ARV) for Category II and III, and use of Immunoglobulin (RIg) for Category III exposures. Commonly encountered exposures include animal injury from the dog bite, cat scratch, bear maul and the ingestion of raw milk from a cow bitten by a suspected rabid dog. All such exposures are considered as risk for rabies. The hospital provides Antirabies vaccine (purified Vero cell Vaccine PVCV) free of cost to all patients but patients pay for Antirabies Immunoglobulin. This study aimed to analyze the direct and indirect costs of rabies post-exposure prophylaxis (PEP) in Kashmir, India.

Methods:

In this descriptive study we analyzed information collected from 429 patients who had suspected rabies exposure and presented to Government Medical College, Srinagar, Kashmir, India. In addition we computed public health expenditure on PEP based on secondary data available at the clinic for year 2016 March to April 2017.

An informed consent was taken from all the participants and in case of minors both consent and assent was taken.

In addition to recording sociodemographic parameters, information regarding costs involved while receiving PEP for rabies was recorded in detail. This was categorized into two groups: direct and indirect, the former including the cost of immunoglobulin, medicines, surgery, travel and consumables such as syringes. Since most of the family members accompanied the exposed person to the clinic to receive PEP, travel cost incurred on accompanying members was taken into consideration.

Loss of wages was taken as indirect Cost. The total cost was estimated as the sum of the direct and indirect cost borne by the patient or the caretaker in case of a minor. In addition, certain

intangible losses were also measured such as the number of school days lost for students and the number of work days lost for those employed. We also calculated the costs incurred on PEP on public health services. Our hospital contribution of 4.3 USD for the anti-rabies vaccine was included in Government costs.

The data were analyzed using SPSS version 20. Results are reported as percentages, mean, median and IQR. The economic status of the patient was assessed by taking into account number of parameters including family size, wage-earning members in the family and below poverty line certification (BPL). The occupation of the victim was taken as a proxy indicator for determining the economic dependency of the victim.

Results:

A total of 429 (n) victims of suspected rabies exposure were included in the analysis. The mean age was 32.5 ±21.1 years and 66.4% were males. The average family size was 6.5 ±4.9SD, with an average earning member of 1.42 ±0.6SD. The most common site of exposure was lower limb 293 (68.3 %) and two third (66.2 %) of the exposures were Class III exposure. More than half of the victims, 239 (55.7%) were economically dependent on their family members. Sociodemographic and exposure characteristics are presented in Table I and II respectively.

Table I: Sociodemographic characteristics of patients attending Antirabies Clinic to receive Post-exposure Prophylaxis.

Sociodemographic parameters	Categories	n (%)
Age (years)#	≤ 9	82 (19.6)
	10-19	58 (13.9)
	20-59	214 (51.2
	>60	64 (15.3)

Gender	Male	285 (66.4)
	Female	144 (33.6)
Residence	Urban	102 (23.8)
	Rural	327(76.2)
Occupation	Employed (private/government)	105 (24.5)
	Students	88 (20.5)
	Petty job/ day earners	85 (19.8)
	Not in any Job*	114 (26.6)
	Not Applicable **	37(8.6)
Income (quartiles) USD	< 108.8	121 (28.2)
	108.81-176.8	95 (22.1)
	176.81-326.4	108 (25.2)
	326.41-2040	105 (24.5)
Below Poverty Line certified		92 (21.4)
Mean Family size (SD)***		6.5 (4.9)
Mean Earning members (SD)***		1.42 (0.63)

*# information on age available for 418 only*Unemployed, home-makers, retired personnel, **not yet in school due to less age.(SD)***(Standard deviation).*

Comment [MC(2]: Define SD as a footnote

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Table II Characteristics of exposure.

Site of bite	Categories	n (%)
	Lower limb	293 (68.3)
	Upper limb	71 (16.6)
	Head and neck	17 (3.5)
	Trunk	13 (3)
	Milk of a rabid animal	8 (1.9)
	Multiple sites	29 (6.8)
Category of bite		
	I	2 (0.5)
	II	143 (33.3)
	III	284 (66.2)
Animal involved		
	Dog	419 (97.7)
	Cow	7(1.6)
	Bear	3 (0.7)

Total cost for five patients could not be calculated as they could not afford the cost of immunoglobulin and other consumables, and hence were excluded when cost estimates were compiled. PEP associated costs are tabulated (Table III).

Table III: Costs incurred on recipients of Postexposure Prophylaxis (in United States Dollars).
The conversion is based on 1 INR equals 0.0136 USD.

Cost heads	Median (Q1-Q3)

Direct cost	20.5 (6.2-29.4)
Immunoglobulin cost	17.1 (8.8-17.1)
Medicine cost	2.7 (0-4.0)
Travel cost	5.4 (2.7-10.8)
Surgical cost	50.8 (39-59.3)
Other consumables (syringe)	0.4 (0.2-0.7)
Indirect cost	20.3 (13.5-24.4)
Wages lost (n=180) USD	
≤ 13.6	59(32.8)
13.61-19.04	34 (18.9)
19.05-23.12	44(24.4)
23.13-81.6	43(23.9)
Total cost	29.3 (10.2-43.1)
Other losses	Mean (SD)
School days lost (n=88)	3.3(1.4)
Work days lost (n=210)	4(0.7)

Cost analysis of PEP at our center for the year 2016 March to 2017 April are tabulated (Table IV). During this period, 6536 victims had suspected rabies exposure and received treatment at our center. We assumed 20% of the recipients were <15 years of age and will need only one vial of RIg(Rabies Immunoglobulin) as per body weight, so total vials of Rig consumed for Category III patients was estimated to be 5926. This assumption was based on the data collected on 429 subjects for this study and clinical observation. The cost calculated for RIg amounted to 50371 USD. The number of vaccine vials consumed to treat 6536 patients (one vial per patient) was 28104 USD. The cumulative cost of treating 6536 patients with PEP (ARV plus RIg) was estimated at 78475 USD.

Comment [MC(3]: Define the acronym in bracket if this is the first time you mentioned it

Alright done

Table IV Cost comparison of Post exposure prophylaxis for Rabies for 6536 victims, who reported to Antirabies clinic from March 2016 to April 2017

Biological	Exposure Category	Cases	Vials	Unit cost *** (USD)	Total Cost*** (USD)	Financial coverage
Vaccines	II	3244	3244	4.3	28104.8	Government

*(PVRV)	III	3292	3292	4.3	(20,91,520 INR)	
**eRIg	III only	3292	5926#	8.5	50371 (37,33,380 INR)	Out of pocket Expenditure
PVRV +eRIg					78475.8 (5,925,380 INR)	

**PVRV (Purified Verocell Rabies Vaccine), **eRIg (Equine Rabies Immunoglobulin)*
#we have assumed 20% of the category III victims are less than 15 years of age and hence need only one vial of Immunoglobulin (20% of 3292=658 need one vial only and rest (3292-658)=2634 need two vials, so total vials consumed=[658+.2(2634)]=5926)
****The conversion is based on 1 INR equals 0.0136 United States Dollar*

Discussion:

Despite being one of the major public health problems in India, national data on mortality and morbidity associated with rabies are meager owing to the fact that it is still not a notifiable disease [13, 15]

In this study, we projected the economic burden of rabies at an individual and healthcare providers level in a government run tertiary care hospital in Kashmir, India, which caters to more than three fourth of suspected exposure to rabies every year in Kashmir. From March 2016 to April 2017, 6536 rabies prone cases were managed at the center. The huge turnover of patients is partially explained by the fact that the hospital is the only well-established antirabies clinic in Kashmir seeing c.50% of all reported cases per annum. Secondly the dog- human ratio of 1:14 in Srinagar is significantly higher than in other parts of India (1:36) [14].

Most affected by canine rabies were from a rural area, and every fifth victim of canine exposure is a child of <9 years. Nationally representative mortality survey and a nationwide epidemiological survey on Rabies in India also identified rural preponderance and most affected population as children less than 15 years in terms of both mortality and

morbidity [15,16].The total cost incurred on PEP was estimated to be 29.3USD.The direct median cost was 20.56 USD and the indirect median cost of 20.3 USD IQR .The wide IQR for total median cost and the direct median cost can be attributed to the costs incurred on surgeries, travel etc ,as some patients had to undergo reconstruction surgery of the damaged part due to severe injury and the travel cost for many patients was reasonably high as they had to travel a large distance to receive PEP.

We came across very few studies seeking to quantify costs related to rabies prevention in this subcontinent. One such study done in Karnataka, a southern state of India has estimated the costs incurred on the management of suspected rabies exposure. They attempted to compare the difference in costs incurred by government and private hospitals. Their findings reveal out of pocket expenditure incurred on PEP in a government setting was only 7.94 USD and the government spending was reasonably high at 13.99 USD, while as, cost of getting PEP in the private hospitals was found to be 70.57 USD in their study [17].On the contrary out of pocket spending on PEP in our setting is more than three times which is very high and needs to be addressed.. The reason for this disparity is attributed to the fact that in Karnataka, government hospitals provide both Antirabies vaccine and immunoglobulin free of cost which greatly reduces the economic burden on the patients. The average immunoglobulin cost in our study was measured at 14.47±4.19 USD. Keeping in view the fact that two third of the victims (66%) had class III exposure who need immunoglobulin as a life saving measure, out of pocket expenditure is tremendous. If the public health spending on PEP expands in our state, the out of pocket expenditure towards immunoglobulin could be cut down to a large extent.

A retrospective study in Southern California to estimate the costs associated with PEP found one-third of the total cost spent on PEP per case was indirect in nature and it was in the form of lost wages, transport, and fee paid for receiving daycare at the treatment facility. They

additionally calculated the indirect cost borne by public health and animal control agencies in the form of the salary of workers, investigation cost to identify rabies virus in animal and travel cost for them. However, their indirect cost estimates included public health cost and animal control activity cost. The mean direct cost equaled 2564 USD (Range 303USD-6455 USD) and Indirect cost equaled 1124 USD (Range 418 USD-2742 USD) [18].

A detailed analysis of monetary expenses and economic impact of rabies compiled for four continents by National Wildlife Research Center(United States Department of Agriculture) reveals startling results. They have figured out approximately 124.2 billion USD is annually spent on canine rabies and more than 80% of annual expenditure on canine rabies occurs in Asia accounting for 832 million USD excluding human mortality cost. Since the data has been projected for four continents there is a lack of true results. Further their estimates are based on arbitrary assumption but they have taken care of uncertainty related to each parameter by using Monte Carlo simulation. Based on this method, they have calculated costs incurred on the management of canine rabies using39 parameters which includes mortality costs in humans and cattle, treatment cost, veterinary and laboratory cost. The average cost of PEP per case is more for Asia 39.21 USD as compared to37.64 USD in Africa. Indirect cost estimates associated with PEP was calculated to be average 0.5 days work missed per visit with 3.85 USD expected income loss per visit, transport cost per visit 4.52 USD [10].

Quite significantly 19.8% of the recipients of PEP suffered from income loss due to the nature of their job which accounted for nearly one week's average income loss which is a substantial amount, keeping in view the level of poverty in India where nearly one third of the population is not able to fulfill their calorie requirements [19]. It was observed, 24.5% of the recipients of PEP did not suffer from loss of wages due to the nature of employment that took care of the opportunity cost of the missed work

Going by the experience from the European region that has successfully eliminated rabies through concerted efforts and robust surveillance mechanism primarily involving mass dog vaccination which has led to the reduction of demand for PEP and subsequent cost associated with it[20-21].

Setting up a system to control animal rabies through collaborative efforts from all stakeholders by advocating mass dog vaccination programme through involvement of veterinarians, management of solid municipal waste through local governance (municipalities and panchayats in urban and rural areas respectively), facilities to quarantine the biting animal with robust laboratory support for testing of animal to rule out rabies in addition to public healthcare services and legal authorities are need of the hour [22,23].

Conclusion:

In the absence of key interventions like mass dog vaccination, quarantine and facilities to check the infection status of the biting animal, the costs of rabies PEP would keep on escalating for individuals as well as public health sector. Keeping in view ethical and legal considerations, dog killing might not be feasible in Kashmir. Other measures of controlling dog population need to be explored. Unlike other parts of India, dog ownership is a big issue in Kashmir because of socio-cultural reasons. Among the zoonotic diseases, rabies remains a primary cause of concern in Kashmir mainly because of the large population of roaming dogs which are unaccounted and has led to an increase in the human animal contact.

1.PEP: Post Exposure Prophylaxis

2.IQR: Interquartile range

3.USD: United States Dollar

4.INR: Indian National Rupees

1. The ethical approval: Ethical clearance for the reported work has been sought from the institutional ethical committee.

2. Competing interests: The authors declare that they have no competing interests in this section.

3. Consent for publication: NA

4. Funding: nil

5. Authors' contributions:

MAQ: Concept, data entry, analysis, report writing.

KB: Data collection, data entry and report writing.

UQ: Data collection and referencing.

SMSK: Discussion

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