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Cost-benefit analysis of controlling rabies: prioritizing areas in rural setting of Maner: a cross sectional study

Nidhi Prasad¹, Binay Kumar²*, Sanjay Kumar Chaudhary¹, Sanjay Kumar¹

¹Department of Community Medicine, IGIMS, Patna, Bihar, India

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*Correspondence: Dr. Binay Kumar,

E-mail: drbinay10@gmail.com

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ABSTRACT

Background: Rabies being a preventable disease with no treatment available once onset starts but can be easily prevented by post-exposure among all animal bite victims. So it is essential to take the full course of vaccination for complete protection.

Methods: The present study was a hospital based cross sectional study and was carried out in rural health training centre in Maner, Patna.

Results: Our study included 340 patients who attended anti rabies clinic for post exposure prophylaxis. Among them 65% were children (<15 years) comprising mostly males (69%) and mostly of category III exposure. Direct cost of post exposure vaccination when compared with the cost of pre exposure prophylaxis is one-third (approx).

Conclusions: Compliance to anti-rabies vaccination for post-exposure prophylaxis is still low and they are still at risk of developing rabies. Reasons being irregular supply of vaccine and immunoglobulin in government hospitals, loss of wages, forgotten dates, cost incurred to buy from outside and distance from the hospital if referred to other centre. Seeing the current scenario, planning and prioritizing areas to achieve our goal and lessen economic burden is need of the hour. We infer that pre exposure prophylaxis may be a cost effective strategy which can aid in the control and elimination of rabies in endemic settings.

Keywords: Post exposure prophylaxis, Equine rabies immunoglobulin, Intramuscular rabies vaccination, Anti-rabies vaccines, Pre exposure prophylaxis

INTRODUCTION

Rabies is an infectious viral disease that is almost always fatal following the onset of clinical symptoms. It is the only disease where prevention is the only cure. Rabies affects both domestic and wild animals.

Incidence of estimated human rabies death in India is around 20,000 and animal bites is 1.7% (17.5 million per year) annually. "National Rabies Control Program" involves two components viz. elimination of human deaths and control of canine rabies to break down the transmission through canine (dog) rabies control. Rabies is one of the neglected tropical diseases that predominantly affects poor and vulnerable populations, particularly children, who live in remote rural locations.² In India, rabies affects mainly people of low socioeconomic status and children between the ages of 5 and 15 years.³ In India true burden of disease is not reflected by the hospital data due to non-reporting, chronic underreporting, poor awareness and political neglect. Community-based systems have good rabies case detection than health system-based reporting. Improved reporting systems are required to address the lack of accurate data and validate these estimates in a number of regions.⁴ Majority (80%) of human deaths occur in rural

²Pathkind Labs, Patna, Bihar, India

areas, where awareness and access to appropriate postexposure prophylaxis (PEP) is limited or non-existent. Although effective human vaccines and immunoglobulins exist for rabies, they are not readily available or accessible to those in need due to shortage of government supply.

It is an irony that most of the expenditure for PEP is borne by those who can least affords it. In developing countries, an estimated 3.87% of the GNP and 31 day wages of an average Asian is spent for full course of PEP.⁵

It is known that \$25 million are spent on post exposure prophylaxis in India annually. ⁶⁻⁸ Because of the high incurred cost on the vaccine and immunoglobulin people cannot afford to get immunized when the government supply is exhausted. Also if they are referred to other centres where vaccine is available they fail to reach due to various constraints like money, large distance and loss of daily wages. Both the availability of biologicals and the costs of seeking PEP are factors in treatment compliance.

So there should be increasing focus on ways to deal with the existing condition. Pre-exposure immunization should also be considered for children living in, or visiting, remote, high-risk areas. Children under 15 years of age have a higher rabies exposure from dogs, as they play with animals, they may receive more severe bites, or may not report bites. WHO continues to promote human rabies prevention through the elimination of rabies in dogs, dog bite prevention strategies, and more widespread use of the intradermal route for PEP which reduces volume and therefore the cost of cell-cultured vaccine by 60% to 80%.

So the study objective is to assess the cost factor for seeking PEP and determine the costs to the government in implementing different combinations of strategies for rabies control and suggest alternatives to the existing system.

METHODS

Study area and population

This study was carried out in Rural Health Training Centre at Maner. The hospital covers a population of 3,16,1256 and covers 19 panchayats. This hospital functions as a referral center, where in various medical practitioners from nearby catchments areas, refer patients suffering from infectious disease to this hospital.

Study design and data collection

This is a cross sectional study based on the anti-rabies register maintained in the anti-rabies clinic of rural health training centre at Maner. The basic profile and details regarding the post exposure prophylaxis of the persons, attended the anti-rabies clinic for first six months from January 2019 to June 2019, was collected from the register maintained at RHTC, Maner. During the data collection period 340 persons attended in the clinic for post exposure prophylaxis. The cost of vaccine (government supply) in our center, per vial of 0.5 ml is Rs. 143. From this we have calculated the amount of vaccine for each person i.e. 0.5 ml as it is given intramuscularly. Equine serum (ERIG) is the only option of immunoglobulin available in the center which costs around Rs. 213 per 5 ml (government supply). This is the rate at which the vaccine and immunoglobulin is available at our center and market prices of both options are higher than this. Since the center is far away from tertiary care center and district hospital, people generally depend on the government supply for vaccine and immunoglobulin. If it is in shortage at certain periods, people don't go outside to purchase it, also on referral to other district hospital due to time constraints and distance, people tend to drop out the subsequent doses of vaccine and do not get post exposure prophylaxis. We have calculated the total amount spent for vaccination serum. Other expenditures like injection, consumables and indirect expenditures such as travel, food has not been calculated.

Data analysis

Data was coded and entered in MS Excel and analyzed. Proportions, means, standard deviations are used in the study.

RESULTS

The total number of persons included in present study is 340 all are either category II or III. The mean age of present study group was 12 years and ranging from 2 years to 80 yrs. Majority of them are below 15 years of age (65%). Majority of the bite cases were reported among males. Likewise, majority of the animal bites was by dogs (90%) followed by cats (9%), jackals (1%) etc. All the animal bite victims who came to the centre were given post exposure prophylaxis which included, rabies immunoglobulin and anti-rabies vaccine Intra-muscular injection as recommended by WHO protocol.

Comparative analysis between the cost of post exposure and pre exposure prophylaxis

Post exposure prophylaxis

Anti-rabies vaccination: Since intra-muscular rabies vaccination (IMRV) is followed at the centre (free of cost), we have taken the amount of vaccine as 0.5 ml per visit and as 5 visit are scheduled day 0, 3, 7, 14 and 28 i.e. total 2.5 ml needed for complete vaccination. From this we calculated the total expenditure incurred for vaccination which comes on an average Rs. 715 per person for vaccination. Total expenditure for IMRV for all 340 persons which presented during study period comes around was Rs. 243100.

Table 1: Cost for post exposure prophylaxis in the study group.

Rabies vaccine used	Amount required (ml) per person	Cost per vial (in Rs.) (Govt. purchased)	Total cost per person (in Rs.)	Total no. of persons taking post exposure prophylaxis	Total cost (in Rs.)
Intra muscular rabies vaccine	2.5 (5 doses given)	143	715	340	243100
Equine rabies immunoglobulin	0.133 per kg	213	426	340	144840
Intra-dermal rabies vaccine	0.8	143	230	340	78200

As IM vaccination/ Equine immunoglobulin is given at our center total cost incurred for post exposure prophylaxis in last six month= Rs. 387940 i.e. \$5622 and if ID vaccination/ is followed cost is 223040 i.e. \$3232.

Table 2: Cost for pre and re-exposure prophylaxis in the study group.

Item	Amount required (ml) per person	Cost per 0.5 ml vial (in Rs.)	Total no. of persons	Total cost (in Rs.)
Pre-exposure prophylaxis(IM)	1.5	143	340	145860
Re-exposure prophylaxis(IM)	1.0	143	340	97240

Total cost incurred for pre exposure prophylaxis in last six month= Rs. 145860 i.e. \$2113 and when re-exposure (if titer is low) is also given the cost is Rs. 243100.

Table 3: Age-wise distribution and gender-wise distribution of dog bite cases reported to centre.

Age distribution	Rural population (no.)	Rural population (%)
Children (<15 years)	221	65
Adult (>15 years)	119	35
Male	235	69
Female	105	31

Mean age (±SD) in years 7.29±2.7.

Rabies immunoglobulin: The dosage of rabies immunoglobulin (RIG) is 40 IU/Kg body weight in case of ERIG and 20 IU/Kg body weight in case of HRIG. As the proportion of immunoglobulin is same in both cases (1 ml contains 300 IU in ERIG and 150 IU in HRIG) the required amount per person is 0.1333 ml/Kg bodyweight. We are taking the cost incurred to govt. agencies in providing ERIG as only this is supplied to the centre. The maximum cost of serum required in the study group was Rs. 144840 with an average cost being Rs. 426 per person in the given study period.

Therefore, the economic burden to the government for the post exposure prophylaxis will be much higher for one year in the whole state. The details regarding the cost for post exposure prophylaxis are given in the Table 1.

Pre exposure prophylaxis

Table 2 shows that if all the 340 persons were immunized with pre exposure schedule before the exposure (pre exposure prophylaxis) then they require only two booster doses of vaccine. So in such cases they require a total of 2.5 ml (1.5 ml for pre exposure prophylaxis and 1.0ml for re exposure prophylaxis) of vaccine. To compare the costs of post exposure prophylaxis and pre exposure prophylaxis, we have calculated the cost of combined pre and re exposure prophylaxis for 340 persons. The cost for

pre exposure prophylaxis was only Rs. 145860 in study group. If we include all for re exposure prophylaxis an additional expenditure for this would be only Rs. 97240. So, the total amount incurred would be Rs. 243100 as immunoglobulin not required in these cases.

In nut shell

As PEP is provided free of cost, the total expenditure to the government was estimated. PEP was provided by Essen regimen and the total amount of vaccine required per person is around 2.5 ml (0.5×5 doses). The cost of one vial of vaccine is Rs.143. Amount of rabies immunoglobulin required was 1 vial (5 ml) for children less than 15 years and 2 vials (6–10 ml) for adults. The cost of equine RIG is Rs. 213 per vial. Hence the government will be spending on an average about Rs. 288 per person for RIGs, considering 65% of the animal bite victims are children below 15 years. Therefore, the total cost for PEP spent by the government is about Rs. 1003, which includes cost of rabies vaccine by intramuscular route and RIG.

Table 3 shows the age and sex distribution of the cases reporting to the center for post exposure prophylaxis. With majority of bite in males (69%), children under 15 years comprised 65% of the total cases reported.

DISCUSSION

Rabies is an economically important zoonosis but neglected disease in India. It is the first zoonosis in the list of neglected diseases targeted for regional and global elimination by 2030. Both, human and animal health sectors have to come together for advocating, and prioritizing investments in rabies control and eventually elimination.² The grave situation in primary-health-care facilities is due to lack of awareness of preventive knowledge of proper post-exposure prophylaxis on the part of many medical professionals, and an irregular supply of anti-rabies vaccine and immunoglobulin by the govt. agencies. In animal sector insufficient dog vaccination, an uncontrolled canine population has jeopardise the situation.⁹

Despite the many recent advances we have a long way to go if we do not plan in light of the existing condition. Information on disease burden can be used to set areas of priorities, allocate resources for disease prevention and assess the impact and cost-effectiveness of interventions to reduce economic burden. 10 Strengthening surveillance of human rabies and information education and communication can take long course. Therefore, in current scenario we would like to describe the extent of the economic impacts of the disease and suggest few areas where with slight modification we can atleast be on the track. This study aimed to calculate costs to the state government in implementing different interventions resulting from illness, deaths and efforts to prevent the disease among the entire rural population of Maner, Patna. Post exposure cost was estimated to be Rs. 387940. So a comparison of this cost was made with the pre exposure cost to see the cost effectiveness. In this study the expenditure for pre exposure prophylaxis was Rs. 145860 (37%) and when re exposure cost was also added it was Rs. 243100 (62%) of the cost of post exposure prophylaxis. Other words this would amount to one-third (approx.) and two-third the cost of Post exposure prophylaxis. Even if booster is needed in case of pre exposure prophylaxis to all study group, it will not cause an economic burden to the government and local population. Further the sensitivity of the equine serum and reduced availability of the immunoglobulin will not be a problem. Therefore pre exposure prophylaxis can be considered as a cost effective intervention for prevention of rabies.

As per recent National guidelines for prevention of rabies in India 2013, dogs are responsible for about 97% of human rabies, followed by cats (2%), jackals, mongoose and others (1%). ¹¹

In our centre also majority of cases are of dog bite, followed by cat bite, monkey bite and jackal in 89:9:1. All animal bite cases of surrounding areas come to this centre, as medical colleges and district hospital is far from this place. There is erratic supply of vaccine and serum at the centre and many times due to lack of

vaccines/serum, the patients are referred to higher centre's that is more than 30 km. Hence patients have to travel long for this vaccine. Then it is difficult to ensure whether they have actually been there to do the same which leads to drop outs and poor compliance. To ensure compliance motivation through proper and behavioural change communication, which requires a lot of investment of time and man power also high cost to government. Most dog bites were in males (69%), and in children up to the age of 15 years (65%).

Although deaths have not the present study highlights the fact that, rabies is most common among adults aged 5-15 years when compared to youth and old age. This might be due to the fact that, 5-15 years age people have more outdoor activity. The age distribution of cases reflects the amount of age-specific exposure to the animals.¹³

The area of concern is due to fear, unawareness or casual attitude of children and parents there is no or late reporting to the center, that raises a big concern as once symptoms are evident, death of patient is inevitable. Though 65% of the patients are children under the age of 15 there is no provision for giving pre exposure prophylaxis in the centre. The Indian Academy of Paediatrics (IAP) has also recommended pre-exposure prophylaxis (PrEP) of children. 14 In this context pre exposure prophylaxis holds great relevance. Another important factor is that though it is safe to inject RIG into bite wounds the problem of pain and anguish specially in children can be avoided with the use of pre exposure prophylaxis. 15 Pre exposure prophylaxis with cell culture vaccine in children has been proved safe. In studies using pre exposure prophylaxis in children, all children achieved adequateviral nuclear antibody concentration of levels above 0.5 IU/ml, which is the required amount. 17,18

PrEP for entire populations are not cost–effective in most settings and is therefore not recommended wide scale. PrEP should be considered in remote settings with limited access to PEP if the annual dog bite incidence is >5%. Our estimated incidence of dog bite from hospital based data in children aged less than 15 year has come out to be 3.4%. So assuming the underreporting we have proposed pre exposure prophylaxis in children less than 15 years. again the decision should be based on strong epidemiological evidence and the local context.5 Where timely access to adequate PEP is not guaranteed and age specific rabies cases are high we can adopt the policies according to the prevailing condition and data available.⁵ The neglected disease indicates that, it is insufficiently addressed by governments and the international community. Hence pre exposure prophylaxis may be considered on voluntary basis. The safety of pre exposure prophylaxis is firmly established. Therefore pre exposure prophylaxis can be considered as a cost effective intervention for prevention of rabies.

It is also stated that the booster doses of rabies vaccines are not required for individuals living in or travelling to high risk areas who have received a complete series of pre exposure prophylaxis with cell-culture based rabies vaccines. 19 The Association of South East Asian Nation (ASEAN) countries adopted a call for action to prevent and control rabies with the goal of elimination by 2020. One of the ways to achieve this goal could be by pre exposure prophylaxis of all infants, children as well as on a voluntary basis. Invariably fatal rabies is preventable with proper prophylaxis and we can be on track to declare it rabies free area. Further studies should be done to analyze the cost effectiveness in different settings to confirm this finding. One limitation in our study is that we have not calculated the indirect expenditure and wastage multiplication of the vaccine and serum. In this study we try to prove that definitely switch over from intramuscular to intradermal route of rabies vaccination may be recommended which reduces both the cost and number of doses needed for PEP, but this can't be followed at our centre because of lack of trained staff and other constraints of storage and monitoring along with very late presentation.20

Therefore, considering the large number of animal bite cases in the country and subsequent increase in the demand for rabies vaccines, universal switch over from intramuscular to intradermal route of rabies vaccination may be recommended which reduces both the cost and number of doses needed for PEP.²⁰ Reduction is by 60% when compared with standard intramuscular vaccination and therefore, largely benefits the poor and needy who visits the Government hospitals. Therefore, it is rationale to introduce intra dermal rabies vaccination in rabies endemic country like India.²¹ In low-resource settings, it is being practiced recently due of its lower cost and high immunogenicity. However, it requires pre requisites to be met. Often patients are advised to watch the offending animal if it is traceable after bite for 10 days before seeking treatment, but as animals can be asymptomatic carriers, there can be risk in delaying treatment. 22,23 To reduce the risk of insufficient dosing as a problem with post exposure, pre exposure can be a good option. Due to challenges in achieving high vaccination coverage among humans and the high costs of existing animal intervention, the policymakers are unlikely to commit to a comprehensive rabies control programme yet.

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Institutional Ethics Committee

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