

## Cost Analysis of Post Exposure Prophylaxis of Rabies in A Tertiary Care Centre- A Cross Sectional Study

Sajna M V<sup>1</sup>, Roshni Culas<sup>2</sup>

<sup>1</sup> Assistant Professor, Department of Community Medicine, Government Medical College, Thrissur, Kerala, India  
<sup>2</sup> Lecturer, Department of Community Medicine

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**Abstract:** India is a rabies endemic country with the highest incidence of rabies cases with approximately 30,000 deaths per year and more than 1,000,000 people undergoing anti rabies vaccination every year. Around 30 to 60% of pre exposure prophylaxis are given to children below the age of 15. The following study was conducted in the district of Thrissur, in the state of Kerala. This study was conducted to analyze the cost of post exposure prophylaxis and to compare assumed cost of pre exposure prophylaxis. Our study included 213 patients attended anti rabies clinic for post exposure prophylaxis. Among the group 63.4% were adults and 36.6% were children. Majority were category III exposure. The analysis of the direct cost of post exposure vaccination was done and compared with the cost of pre exposure prophylaxis. The post exposure vaccination included 4 doses of Intra dermal rabies vaccination –two site regime (modified Thai red cross regime) along with rabies immunoglobulin for category 3, added up to \$ 4540. This was compared with the cost that would have occurred if these patients had previously received pre exposure prophylaxis which was \$890. It was found that Pre exposure prophylaxis came to only to one fifth the cost of post exposure prophylaxis. We infer that Pre exposure prophylaxis is a cost effective strategy which can aid in the control and elimination of rabies in endemic countries.

**Key Words:** Post Exposure prophylaxis, intra-dermal rabies vaccination, Equine rabies immunoglobulin, Human rabies immunoglobulin.

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### I. Background

Rabies is the 10<sup>th</sup> biggest cause of death due to infectious diseases worldwide (1). Out of the total number of Rabies cases, 95% of human Rabies deaths occur in Africa and Asia. Among this, 36% occurs in India (2). Rabies is endemic in India and approximately 30,000 people die of the disease every year and more than 10,00,000 people undergo anti-rabies vaccination every year. Every two seconds, one person is bitten by a dog in India. Across Asia the annual expenditure due to rabies is estimated to be reaching 563 million USD (3). It is known that \$25 million are spent on Post Exposure Prophylaxis in India annually (4-6). Around 40% of Post Exposure Prophylaxis is given to children below the age of 15yrs.

Rabies typically affects the most vulnerable members of society, children and lower socio-economic classes. This is likely due to poor knowledge and uptake of preventive measures. The psychological impact of fear and trauma after a suspected rabid dog bite is difficult to translate into a monetary value but was estimated to account for about 32,000 disability-adjusted life year (DALYs) in Africa and 1,40,000 DALYs in Asia (7). According to WHO recommendation in 2010, routine immunization (Pre exposure prophylaxis-PREP) against Rabies for children in high risk population with a follow up booster every five years is advised.

Animal exposures can be divided to three categories according to World Health Organization. Prophylaxis can be post exposure prophylaxis (PEP), pre exposure prophylaxis (PREP) and re exposure prophylaxis. Pre exposure prophylaxis consists of vaccination on 0-3- 21/28<sup>th</sup> days. Usually this is given to only high risk persons. All category II and III animal exposures have to take post exposure prophylaxis. Wound washing, active immunization and passive immunization is necessary to prevent rabies. Anti rabies vaccines are required in both the exposures in category II and III but the rabies immunoglobulin is required only in category III exposure. There are two types of vaccination schedules viz, Essen schedule (intra muscular on days 0-3-7-14-28) and Updated Thai Red Cross regime (intra dermal injection of 0.1ml on two deltoids on days 0-3-7-28). The dose of vaccine is same to all. The total amount of intradermal vaccine per person is 0.8 ml and intramuscular vaccine is 2.5 ml per person. The amount of immunoglobulin depends on the weight of the patient. Maximum dose is 10 ml. There are two types of immunoglobulin available, i.e. equine rabies immunoglobulin (ERIG) and human rabies immunoglobulin (HRIG). Equine serum is associated with anaphylactic reactions due to equine origin. Human immunoglobulin is costly when compared with equine. (Treatment schedule is given in the table number. 1)

In Kerala, Intradermal schedule (Updated Thai Red Cross regime) of rabies vaccination was implemented in 2009. This vaccination is implemented in all levels of health care centers. Intradermal rabies

vaccination and equine rabies immunoglobulin are free of cost to all irrespective of their economic status in Kerala. If there is sensitivity to equine serum, the patient has to take human rabies immunoglobulin which should be afforded by the patient himself. On an average 60 – 80 patients are attending in a tertiary care centre for prophylaxis of rabies. Government is spending a large amount for post exposure prophylaxis.

This study was conducted with the objectives to analyse the direct cost of the post exposure prophylaxis of rabies in a tertiary care centre by the Government and to compare the cost of Post exposure and assumed cost of Pre exposure Prophylaxis.

## II. Materials And Methods

This is a cross sectional study based on the anti rabies register maintained in the anti rabies clinic of Government Medical College Thrissur, Kerala, India. The basic profile and details regarding the post exposure prophylaxis of the persons, attended the anti rabies clinic for first week of May 2013, was collected from the register maintained in the anti-rabies clinic of Department of Community Medicine. During the data collection period 213 persons attended in the clinic for post exposure prophylaxis.

The cost of vaccine (Government price) per vial of 0.5ml is taken Rs.250. The market prize is higher than this. From this we have calculated the amount of vaccine for each person i.e. 0.8ml. Equine serum (ERIG) costs around 433 Rupees per 5ml in the market. But we have taken as Rs 400/ vial (reduced rate). We have calculated the required amount (in ml) of serum for each patient and thus obtained the cost. If the patient was given human rabies immunoglobulin (HRIG) the cost is different. There were two brands of HRIG available in the market which costs Rs 2763 per vial (2ml) and Rs 6432 per vial (2ml) respectively. We used to give both the types of HRIG depending upon the availability in the vicinity of the College.

We have calculated the total amount spent for vaccination and serum. Other expenditures like injection consumables and indirect expenditures such as travel, food has not been calculated. As this is a tertiary care centre and we are maintaining a 24 hour clinic for post exposure prophylaxis the wastage for the vaccine and serum is minimal.

**Data Analysis:** Data was coded and entered in MS Excel and analyzed using SPSS .16 software. Proportions, means, standard deviations are used in the study.

## III. Results

The total number of persons included for the study was 213. Mean age of the group was 30.19±20.1years ranging from 2years to 80 years. Majority were above 15 years of age (64.3% n=137) and the rest below 15 years (35.7%). Among the study population 135(63.4%) were males. Regarding the type of exposure, category III was maximum number 188(88.3%) followed by category II, i.e 23(10.8%) and category I (n=2). Exposure to dog (63%) was high compared to cat (28%) and other animals (8.4%). The requirement of intra dermal rabies vaccine is similar in all except in 6 persons who has undergone re exposure prophylaxis.

### Cost of Post Exposure Prophylaxis:

**Anti Rabies Vaccination (Idrv):** Among the study group, 6 persons were previously vaccinated and hence they required only two booster doses of vaccine. Re exposure prophylaxis consist of two doses of vaccine on days 0 and 3. Only 0.1 ml of vaccine per dose is required (a total of 0.2ml) in case of intradermal vaccine schedule. Since intra dermal rabies vaccination is followed in the centre, we have taken the amount of vaccine as 0.2ml among these 6 persons. All other persons needed 0.8ml for active immunization. We have calculated the total expenditure incurred for vaccination for 1 week period. Average cost per person for vaccination was Rs 391.5. Total expenditure for IDRV in the institution for one week was Rs 83,400 (\$ 1383.77).

**Rabies Immunoglobulin (Rig):** The dosage of immunoglobulin 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 0.1333ml/Kg bodyweight. Average amount of serum required was 5.9± 2.4 ml. The maximum cost of serum required in the group was Rs 50350 (\$843.67) with an average cost being \$34.68. Total expenditure for immunoglobulin in this institution for one week was Rs 1, 90,214 (\$ 3156.03).

Thus the total direct expenditure for post exposure prophylaxis for one week was Rs 2,73,614 (\$ 4539.81). This is only for one week in this centre. 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 number 2.

### Comparison between Costs of Post Exposure Prophylaxis and Pre Exposure Prophylaxis

We have assumed that if these 213 persons were immunized prior to the exposure (Pre exposure prophylaxis) they require only two booster doses of vaccine. Rabies immunoglobulin is not required among

these persons. So in such cases they require a total of 0.5ml (0.3ml for Pre exposure prophylaxis and 0.2ml for re exposure prophylaxis) of vaccine. In order 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 213 persons. The cost for pre exposure prophylaxis was only Rs 31,950 (\$ 530.11) in 213 persons. If they had undergone re exposure prophylaxis an additional expenditure would be only Rs 21,550(\$ 358.69). So the total amount incurred would be Rs 53,500(\$ 890.48). Details are given in the table no 3. Comparison of the total costs between the two types is given in the figure no 1.

#### **IV. Discussion**

India is reported to have the highest incidence of rabies globally. National Multi centric Rabies Survey, conducted in 2003 by the Association for Prevention and Control of Rabies in India in collaboration with the World Health Organization reported that there were 20, 565 deaths from rabies per year. Most rabies deaths were in males (62%), in rural areas (91%), and in children below the age of 15 years (50%). (7, 8). 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%). (9). It is reported that there are approximately 25 million dogs, with an estimated dog: man ratio of 1:36 in India(10). Our Medical College is situated in Central Kerala, in the Southern tip of India. Kerala ranks first in Health indicators with Literacy rate of 93%, in comparable with developed countries. The people are very health conscious.

All category III animal bite cases in the state are referred to tertiary care centres for giving anti rabies serum, as competent staff is required for the administration and management of anaphylactic reactions of the serum. The number of Government Medical colleges is less in Kerala. Hence patients have to travel long for administering the life saving drug in post exposure prophylaxis of rabies. The serum should be administered as soon as possible in the local wound site to prevent local multiplication and attachment of virus to the nerve endings. At times there can also be unpredictable shortage of ERIG and HRIG. High costs, importation of HRIG are some of the important causes of limited supply in the Government hospitals.

In this study the expenditure for pre exposure prophylaxis is only 19.5% of the cost of post exposure prophylaxis. Other words this would amount to one – fifth the cost of Post exposure prophylaxis. Even if there is need for booster doses of vaccine in case of pre exposure prophylaxis, it will not cause an economic burden to the Government and general population. Further the sensitivity of the equine serum and reduced availability of the human 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 rabies prophylaxis in India 2013, (9) Pre-exposure vaccination may be offered to high risk groups like laboratory staff handling the virus and infected material, clinicians and persons attending to human rabies cases, veterinarians, animal handlers and catchers, wildlife wardens, quarantine officers and travellers from rabies free areas to rabies endemic areas. Only high risk categories such as veterinary and forest staff are given pre exposure prophylaxis against rabies currently. Though 40% of the patients are children under the age of 15 there is no provision for giving pre exposure prophylaxis in the state. The Indian Academy of Paediatrics (IAP) has also recommended pre-exposure prophylaxis of children (11). In this context pre exposure prophylaxis holds great relevance. Another important factor is that though it is safe to inject RIG into bite wounds (12) the problem of pain and anguish especially in children can be avoided with the use of pre exposure prophylaxis.

Pre exposure prophylaxis with cell culture vaccine in children has been proved safe (13). In studies using Pre exposure prophylaxis in children, all children achieved adequate viral nuclear antibody concentration of levels above 0.5IU/ml, which is the required amount. (14,15 ).Hence Pre exposure prophylaxis may be considered on voluntary basis. The safety of Pre exposure prophylaxis is firmly established. Only two documented cases of seroconversion failures have been observed among Pre exposure prophylaxis receivers especially in immuno-compromised persons(15,16 ).Chulasugandha P et al found that costs of both strategies, Pre exposure prophylaxis of children or PEP of exposed, become equal when the dog bite incidence is 2-30%; depending on which post-exposure treatment regimens (PEP) are used in study conducted in Thai children (17)

The annual birth rate in Kerala is low (14.7 as per 2011 census) and the immunization coverage is high. Pre exposure prophylaxis may be implemented in a phased manner as the immunization schedule advised by WHO and IAP (18).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 (18,19).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 makes it rabies free area. Further studies should be done to analyse 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.

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**Table no: 1.** Treatment schedule of animal bite cases

Category	Type of Exposure	Treatment
Category I	Touching or feeding animals, licks on the skin	Local treatment
Category II	Nibbling of uncovered skin, minor scratches or abrasions without bleeding, licks on broken skin	Local treatment, Anti rabies vaccine
Category III	Single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks; exposure to bat bites or scratches	Local treatment, Anti rabies vaccine, Rabies immunoglobulin

**Table number 2:** Cost for post exposure prophylaxis for the study population

Item	Amount required (ml) per person	Cost/ Vial (Rs)	Cost/ person (Rs)	Total number of persons taken post exposure prophylaxis	Total cost (Rs)	
Intra-dermal rabies vaccination	Post exposure prophylaxis	0.8	250	400	207	82,800
	Booster dose (re exposure cases)	0.2	250	100	6	600
Equine rabies Immunoglobulin	0.133/kg	400	Maximum 800	210	83920	
Human rabies Immunoglobulin	0.133/kg	2500-6400	Maximum 6400	3	1,06,294	
<b>Total cost incurred for post exposure prophylaxis for 1 week = Rs 2,73,614 i.e. \$ 4539.81</b>						

**Table number 3:** Cost for pre and re exposure prophylaxis for the study population

Item	Required amount(ml)	Cost /Vial (0.5ml) in Rs	Total Persons	Total Cost (Rs)
Pre exposure prophylaxis	0.3	250	213	31,950
Re exposure prophylaxis	0.2	250	213	21,550
<b>Total cost incurred</b>				<b>53,500 (\$ 890.48)</b>

**Fig no2.** Comparison of cost of Post exposure with pre exposure prophylaxis

