

Original Research Article

Cost analysis of rabies prophylaxis in India

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ABSTRACT

Background: Rabies, a viral zoonotic disease is the 10th biggest cause of death due to infectious disease worldwide. This study was conducted to analyse the cost of post exposure prophylaxis and to compare the cost of post exposure prophylaxis with assumed cost of pre exposure prophylaxis.

Methods: Current index of medical stores (CIMS), and online literature were used to review the prices of anti-rabies vaccine (ARV) in market. Cost for different categories was compared for 60kg person. Percentage cost variation was calculated to find the cost variation among ARV brands.

Results: The cost of post exposure vaccination as per Essen regimen was approximately Rs.2000 and including immunoglobulin for category 3, added up to Rs. 22,894 for a 60 kg person. This was compared with cost of pre exposure prophylaxis which was found to be Rs. 1050-1200. It was found that PrEP was 20 times lesser than the cost of PEP.

Conclusions: We infer that pre exposure prophylaxis is a cost effective strategy which can aid in the control and elimination of rabies in endemic countries. Health education activities should be intensified towards pre exposure vaccination among pet owners, in areas with high population of dogs and also in vulnerable group.

Keywords: Cost variation, Dog bite, Prevention, Pre exposure, Post exposure

INTRODUCTION

Rabies has terrified man since antiquity. Rabies is an acute, highly fatal viral disease caused by Lyssavirus type 1, affecting the Central Nervous System.¹ Rabies is a viral zoonotic disease transmitted to humans through the infected saliva of certain animals including dogs, wolves, foxes, jackals, cats, lions, bats, monkeys and humans.² Most of human deaths follow a bite of an infected dog.³ Classical hydrophobia is clinically characterised by a variable incubation period, a short period of illness due to encephalomyelitis ending in death, despite intensive care. Rabies is the only communicable disease of human that is always fatal.¹

As per WHO data more than 2.5 billion people are at risk in over 100 countries reporting the disease.⁴ Rabies ranks the 10th biggest cause of death due to infectious diseases.⁵ Rabies is a vaccine preventable viral disease and is prevalent in more than 150 countries.⁶ Nearly 55,000 deaths occur each year mostly in Asia and Africa. The incidence of animal bites is 17.4 per 1000 population. A person is bitten by a dog every 2 seconds, and someone dies from rabies every 30 minutes.² India being endemic for rabies accounts to 36% of world deaths and approximately 18,000-20,000 deaths each year of which 30 -60% are children less than 15 years of age.⁶

Rabies can be transmitted when infectious material with rabid dog saliva comes into direct contact with human mucosa or fresh skin wounds. Incubation period of this

disease is variable, commonly 1 to 3 months after exposure. The incubation periods usually depends upon the site of bite, severity of bite and number of wounds, viral load, etc. Rabies in human begins with prodromal symptoms like headache, malaise, sore throat and fever. Nearly 80% have pain, tingling sensation over site of bite. This stage is followed by excitation and stimulation of nervous system involving sensory, motor, sympathetic and mental system in an order. Patient shows pathognomic signs of aerophobia (fear of air) and in later stages develop hydrophobia (fear of water). Duration of illness is 2 to 3 days.¹

Patient may die abruptly during convulsions or may pass on to paralysis and coma leading to death. On examination, there will be increased reflexes and muscle spasm along with pupil dilatation and increased perspiration, salivation and lacrimation. Rabies can be confirmed by antigen detection using immune fluorescence of skin biopsy and by isolation of virus from saliva and other secretions. Patient should be isolated, treated with anti anxiety drugs, proper hydration and diuresis followed by intensive therapy as respiratory and cardiac support are given.¹

All though rabies is 100% fatal, it is a vaccine preventable disease. Vaccination against rabies is usually done under the following circumstances⁷ like pre exposure vaccination which is given to protect at risk group and Post exposure vaccination to prevent rabies after an animal bite suspected with rabies. The WHO has categorised rabies exposure into three categories.⁸

Category I is no exposure stage which includes touching or feeding animals and animal licks on intact skin; Category II is exposure phase involves nibbling of uncovered skin, minor scratches or abrasions without bleeding and Category III is in severe exposure phase there can be single or multiple trans-dermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal lick or direct with bats.

Various treatment regimens are followed for rabies vaccination. For pre exposure prophylaxis 3 doses of anti rabies vaccine is administered as intramuscular injection on 0-7-21 or 28 days as 1 dose per day.

In case of post exposure prophylaxis 2 types of regimen are followed, namely, Essen regimen and Zagreb regimen. Former comprises of 5 dose of IM injections on 0-3-7-14-28 days while the latter is 4 dose multisite regimen which includes 2 doses on day zero followed by 1 dose each on day 7 and 21 respectively.⁸

Management of dog bite

Washing wound thoroughly with soap and water is the first line of management followed by applying povidone iodine. Immunization is the second line management for

which Anti-Rabies Vaccine is given for active immunization and rabies immunoglobulin is given for passive immunization.⁸

Active immunization

Vaccines can be administered either Intra-Dermal (ID) or Intra-Muscular (IM) route. ID injection sites are the deltoid, antero lateral aspect of thigh or supra scapular regions whereas the recommended site for IM administration is the deltoid for adults and children aged more than 2 years, and the antero lateral aspect of thigh for children aged less than 2 years.⁹

In Tamil Nadu, government sectors administer vaccine as ID route whereas the private sectors practice IM administration.⁷ In India rabies vaccines are derived from Purified Vero cell Rabies Vaccines (PVRV), Chromatographically Purified (PVRV), Purified Chick Embryo Cell Vaccine (PCECV) and Purified Duck Embryo Vaccine (PDEV) which costs about Rs.334, Rs. 315, Rs. 349 and Rs. 256 respectively.

Passive immunization

In India there are two types of Rabies Immunoglobulins (RIG) available, Equine RIG and Human RIG. Equine immunoglobulin is heterologous in origin which are produced from hyper immunization of horses and human rabies immunoglobulin are homologous in origin and are comparatively costly. The dose of these immunoglobulin are 40 IU per kg body weight and 20 IU per kg body weight respectively.⁹ In India three brands of Human rabies immunoglobulins are available which is priced about Rs.5715 and Equine immunoglobulin costs around Rs.600.

Globally, the cost of anti-rabies vaccine amounts to Rs. 36 million and when given along with immunoglobulin summed up to amount of Rs 119 million annually.¹⁰ Since 2004, each patient required at least 4 visits for treatment, at a cost of Rs 3500 for the vaccine and other medicines. Earlier most of the patients either did not receive any vaccination or did not complete the course.²

There is a shortage of anti -rabies vaccine in India , not because of lack of the production but due of export of vaccines.¹¹ Tamil Nadu has maintained an adequate stock of ID vaccine injections which are given free of cost.¹² On the other hand production of Rabies immunoglobulin remains inadequate in India.¹³

With this background this study was planned to figure out the cost variation among various brands of anti-rabies vaccines in India and the cost analysis of rabies prophylaxis used in the treatment of various categories of animal bite.

METHODS

Study design

This record based study was done with information from various sources like CIMS, online literature and vaccine price register records from hospital settings to calculate the cost variation of rabies prophylaxis in India.

Study period

Study was conducted over a period of 6 months, from November 2019 to April 2020.

Study setting

Sree Balaji Medical College and Hospital and other Government linked hospitals treating animal bite cases in Chennai.

Data collection

Current Index of Medical Stores (CIMS), and online literature were used as information guide to review the prices of various brands of Anti-Rabies Vaccine (ARV) used in the treatment of animal bite.¹³

Statistical tools and statistical analysis: Simple mathematical tools like cross multiplication and others were used and data represented in form of tables and charts.

Cost variation of the vaccines manufactured by different pharmaceutical companies was calculated as percentage cost variation using the following formula.

Percentage cost variation = $\frac{\text{Maximum cost} - \text{Minimum/Minimum cost}}{\text{Minimum cost}} \times 100$

The direct cost of post exposure vaccination for different categories of animal bite (for a person weighing 60 kg) was calculated and compared with the cost of pre exposure prophylaxis.

RESULTS

Cost analysis of Post exposure prophylaxis (PEP)

The assumed cost analysis of post exposure prophylaxis for a 60 kg person is depicted in Table 1. As per Essen regimen, a 60 kg person should be treated with more than 2.5 IU of anti-rabies vaccine as 5 doses intramuscularly. This would require 5 vials of anti-rabies vaccine. Considering the cost of one vaccine vial to be Rs.350, the total cost of 5 doses of anti-rabies vaccine will be Rs.1750. On treating the person with Equine rabies immunoglobulin at a dose 40IU/kg.

About 8 vials containing 300IU (5 ml) of equine immunoglobulin each will be required to treat a 60 kg person which will sum up to a cost of Rs. 5080, with the cost of one vial being Rs.635. On the other hand, human rabies immunoglobulin is used at a dose 20 IU/kg per person. A total of Rs.21,144 will be required to treat a 60 kg person, as 4 vials (each vial containing 300IU) each pricing to Rs.5286 will be necessary.

Cost analysis on treatment basis

The cost analysis of rabies treatment as per categories is illustrated in Table 2. Pre exposure prophylaxis is administered as three full intramuscular dose of anti-rabies vaccine given on 0, 7, 21 or 28 days.⁷ Assumed cost of one vial is Rs.350, thereby the cost of pre exposure prophylaxis will be approximately Rs.1050. In addition to this, 2 doses of anti-rabies vaccine will be required for re exposure prophylaxis leading to a total cost up to Rs.1750. As per Essen regimen, category 1 does not require any vaccination as wound washing is sufficient. Category 2 includes 5 complete doses of anti-rabies intramuscular vaccination which costs to Rs.1750. In addition to 5 doses of ARV, category 3 can be treated either with equine immunoglobulin or human Rabies Immunoglobulin, which costs up to Rs.6830 and Rs.22,894 respectively.

Table 1: Cost analysis of post exposure prophylaxis (PEP).

Injection	Dose per person	Cost/vial	No. of vials	Cost/person (60kgs weight)
ARV IM	≥ 2.5IU	Rs 350	5	Rs.1750
Equine rabies Ig	40 IU /kg	Rs 635	8	Rs.5080
Human rabies Ig	20 IU/kg	Rs 5286	4	Rs.21,144

Ig: Immunoglobulin, ARV: anti rabies vaccine, IM: intramuscular

Table 2: Cost analysis of pre, re and post exposure prophylaxis.

Categories	Treatment	Cost in rs for 60kgs
Pre exposure [PeEP]	3 Doses of ARV	1050
Re exposure [ReEP]	PrEP + 2 doses of ARV	1750
Post-Exposure [PEP]		
Category 1		None
Category 2	Wound management , ARV (ESSEN REGIMEN – 5doses)	1750
Category 3	Wound management + ARV +Equine RIG	6830
	Wound management + ARV+ Human RIG	22894

Cost comparison of treatment modalities

The assumed cost of various treatment modalities for rabies is illustrated in Figure 1. The cost of re exposure Prophylaxis (Rs.1750), PEP with equine (Rs. 6830), PEP with Human RIG (Rs. 22894) are 1.7, 6.5, 22 times more when compared with the cost of pre exposure prophylaxis (Rs.1050).

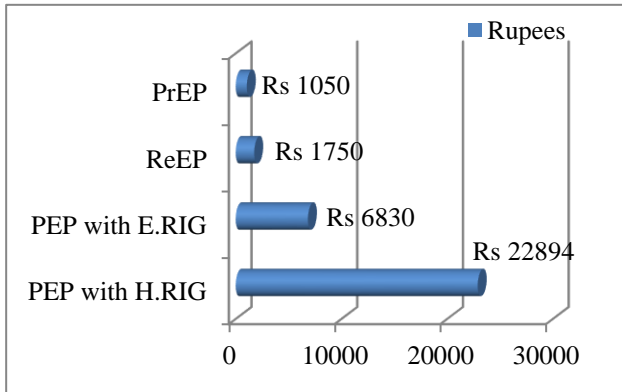


Figure 1: Cost comparison of pre and re exposure with post exposure prophylaxis.

Percentage cost of variation among various brands of ARV available in India

List of various anti-rabies vaccine brands available in India are tabulated in Table 3 to calculate the percentage cost variation of anti-rabies vaccine. Price ranged from Rs.315 to Rs.351. The percentage cost variation was calculated to be 13.2 % which shows that there is very less cost difference among the 7 brands of ARV which are currently available in India.

Table 3: Percentage cost variation of anti-rabies vaccine.

Brands	Cost in rupees
Brand 1	Rs 350
Brand 2	Rs 315
Brand 3	Rs 349
Brand 4	Rs 351
Brand 5	Rs 325
Brand 6	Rs 337
Brand 7	Rs 310

Percentage cost variation is 13.2%.

DISCUSSION

Rabies is one of the oldest viral zoonotic disease recognised in India since the Vedic period (1500-500BC). Rabies is considered as a mammalian disease with dog being the main reservoir.² Dog bite contributes to nearly 99% of human transmission.¹⁴ In India there are nearly 59.9% rabies deaths and up to 35% deaths globally.¹⁵

Annually around 59000 human deaths are estimated worldwide of which 95% occurs in Africa and Asia.¹⁴ In India 18000 to 20000 human deaths occur due to rabies each year.¹⁶ Studies being conducted in various states of India suggest the incidence of rabies to be 2-19 per 1000 person annually.¹⁷ A report from Centers for Disease Control and Prevention highlights that one person dies of rabies every 9 minutes.¹⁸

Rabies in human has clinically two forms, the paralytic form and the furious form. The paralytic form accounts for nearly 20% of the human cases where the person presents with paralysis of the muscles gradually leading to coma. Whereas in the furious type, victim presents with signs of excitable behaviours, hyperactivity, hydrophobia and aerophobia, all of which gradually lead to cardio respiratory arrest.¹⁴ Rabies infection is 100% fatal once the symptoms appear.¹⁹ Even though rabies has a high case fatality rate, it is a vaccine preventable disease.¹⁴

Rabies being one among the neglected tropical diseases, predominantly affects the remote and rural population. In spite of being a vaccine preventable disease, availability and accessibility of the rabies vaccines and immunoglobulin remains a challenge for those in need.¹⁴ The gradual rise of rabies cases and the demand for vaccination raises the question on whether rabies in dogs is epidemic in India or whether this reflects the increased exposure of humans to dog bite.² It can also be due to non availability or non accessibility to vaccines, at the needed time.

Thorough cleansing of the wound and immediate vaccination can prevent the onset of the disease. Anti rabies vaccines are delivered either as intra dermal or intramuscular routes. Intra dermal regimens are fractional dose of intramuscular vaccine. Both the vaccines used are same, but route, dose and site may differ. Government sectors provide anti rabies vaccine as intra dermal route as this allows wide coverage of prophylaxis thus making it cost effective. On the other hand anti rabies vaccines are paid and administered as intramuscular route in private sectors thereby creating the demand and escalation of cost.

From WHO data, it is estimated that full course 5 vials for intramuscular post exposure prophylaxis rounds up to a sum of Rs.7127.²⁰ Whereas for intra dermal route 2 vials are sufficient offering equal safety and efficacy. This shows that intra dermal schedules are cost effective. By shifting from intramuscular to intra dermal countries can overcome vaccine shortage, improve availability, improve affordability of vaccines and provide equitable access to PER, thereby reducing rabies mortalities worldwide by 2030.²⁰

However in India private sectors prefer intramuscular over intra dermal for various reasons like availability of trained staffs, adequate cold chain facility for storage of

vaccine, adequate supply of suitable self-mounted intradermal syringes, open vial and safe storage practices and to avoid the complications like local reactions, fever etc.⁹

A newspaper article states that shortage of rabies vaccines in India has led to increase in price of vaccine to double the amount. Thereby the cost of post exposure prophylaxis requiring 5 vials leads to cost of approximately Rs 2000. Though India produces 50 million vaccines annually, almost 30% of which are being exported, therefore leading to shortage of anti rabies vaccine in India.¹¹ Because of this reason India is running short of 13 million vaccines annually.

From this study, it can be seen three vials of anti rabies vaccine are required for pre exposure vaccination which sums up to cost of Rs 1050, which is 6 times lesser when compared with the cost of treating a patient with post exposure anti rabies vaccine that includes 5 vials of anti rabies vaccine when given along with equine immunoglobulin, and almost 22 times lesser if treated with 5 vials of anti rabies vaccine and human immunoglobulin. By this we can infer that pre exposure vaccination of the high risk group is cost effective method.

Apart from the pre exposure vaccination, we also calculated the cost of re exposure vaccination. In case of dog bite event among those who are previously vaccinated, the additional cost of re exposure vaccination will be Rs 700. Policy makers and other program planners can consider this long-term financial sustainability before implementing as state or national wide control program.

Even though vaccines and immunoglobulin prevent from disease, education plays a vital role for rabies prevention. Creating awareness among the communities, targeting children on how to avoid dog bites can be a key to prevent rabies. Insisting of thorough wound washing with soap and water immediately after the bite is life saving.¹⁹

In a study done by Megan in Tamil Nadu based on One Health Committee Approach, highlights that, in addition to the post exposure prophylaxis to humans following dog bite, canine vaccination and sterilization can be practiced. Canine vaccination can also be yet another cost effective method.²¹ Technological improvements like MISSION RABIES which is a smart phone app lays platform for reporting of dog bites and suspected rabid animals targeting over mass dog vaccination. By this way nearly 1,306,604 dogs are vaccinated.²² Having recently given recognition to National Rabies Control Program, it is important that these methods adopt long term perspectives before developing global rabies elimination strategy.¹⁰ The limitations of this study are that this study was not conducted on any specific population. There might be better results if similar study was conducted with a specific sample size and followed up.

CONCLUSION

We infer that pre exposure prophylaxis is a cost effective strategy which can aid in the control and elimination of rabies in endemic countries. Health education activities should be intensified towards rabies prevention. Pre exposure vaccination among pet owners in areas with high population of dogs and also in vulnerable group like children less than 15 years of age, diabetic and elderly can reduce incidence of rabies. Rabies deaths in human are preventable through prompt vaccination. Vaccinating dogs is the most cost-effective strategy for preventing rabies in people. Information Education and Communication programs should be strengthened towards creating awareness on how to avoid rabid dogs, treatment seeking behaviour and how canine vaccination can interrupt rabies transmission.

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