

# Compliance of Post-Exposure Prophylaxis of Anti-rabies Vaccine amongst Animal Bite Cases Attending Secondary Healthcare Hospital in Thiruvallur District, Tamil Nadu, India: A Cross-sectional Study

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## ABSTRACT

**Introduction:** India has the highest burden of animal bite cases globally, with a large proportion of the population affected by dog bites. India is endemic for rabies and accounts for 36% of the world's rabies deaths. Mortality can be prevented by Post-Exposure Prophylaxis (PEP) with effective vaccines that are available. Vaccines are provided free of charge in Government hospitals.

**Aim:** To estimate the compliance rate of Anti-Rabies Vaccine (ARV) regimen managed by the intradermal route.

**Materials and Methods:** This was a cross-sectional record-based study from the ARV Register of Government Hospital, Gummidipoondi, Tamil Nadu, India. The victims of animal bite cases attending the hospital for the ARV regimen for a month

were selected from the register to assess adherence to the full course updated Thai Red Cross regimen and identify any constraint factors hindering them from completing the course.

**Results:** Out of 108 patients, 79 completed the full course ARV regimen, resulting in a compliance rate of 73.1%. Factors such as the distance of the hospital, timings, and forgotten dates were identified as major constraints.

**Conclusion:** The compliance rate was found to be moderate, with constraint factors like forgotten dates and the distance of the hospital being significant hindrances to compliance. This highlights the importance of strengthening awareness through sensitisation programs and health education in both urban and rural areas to achieve a rabies-free India.

**Keywords:** Adherence, Constraints, Dog bite

## INTRODUCTION

Rabies is a vaccine-preventable zoonotic disease. The rabies virus belongs to the family *Rhabdoviridae* and genus *Lyssavirus*, which is transmitted through bites, licks on broken skin, scratches, and mucous membranes. Apart from a direct bite, the saliva of unimmunised dogs and cats also has the potential to transmit rabies. Human rabies cases have also been documented following corneal transplantation and solid organ transplantation from a misdiagnosed rabies patient [1]. Upon entry, the virus spreads neurotropically, multiplying at the site of inoculation (such as muscles) or entering peripheral nerves, traveling via retrograde axoplasmic flow to the central nervous system before reaching the brain. In the brain, the hippocampus, cerebellum, hypothalamus, and scattered neurons in the reticular formation are the main areas involved in the pathogenesis of the disease. The clinical features consist of three phases: the Prodromal phase (numbness and tingling sensation in limbs, malaise, sore throat, increased temperature, priapism, and headache), the Excitation phase (fear of water (hydrophobia), pharyngeal and laryngeal spasms, terror and excitement, cardiac arrhythmias, respiratory arrhythmias, hypertension, intense thirst and dehydration, fear/convulsions on exposure to light, air and sound), and the Paralytic phase (flaccid and limp muscles, convulsions, unconsciousness). The average incubation period ranges between 30-90 days. Due to this longer incubation period, it is possible to institute PEP in patients who report late. Although rabies affects all age groups, children are the most vulnerable, constituting 40% of those exposed to dog bites [2].

The number of dog-mediated rabies deaths is estimated to be 59,000 annually worldwide, with Asia (59.6%) and Africa (36.4%) bearing the highest burden. In India, which accounts for 96% of morbidity and mortality due to animal bites in the country [2], the National Rabies Control Programme (NRCP) has developed a multisectoral collaborative plan known as the "National Action Plan for Dog-Mediated Rabies Elimination (NAPRE)." Various states across India are working towards this plan to eliminate rabies from the country by 2030 [2]. The three components in the management of dog bites include the management of animal bite wounds, active immunisation with the ARV, and passive immunisation with Rabies Immunoglobulin (RIG). The World Health Organisation (WHO) estimates that India contributes to 36% of global rabies deaths [3]. While there is expected to be a decline in the number of dog bite cases in the near future, it is essential to take adequate measures for the complete elimination of rabies [4]. Although vaccines are available free of cost in government hospitals today, there is an increasing demand to motivate animal bite victims to complete the full course of vaccination by healthcare professionals and to address the constraints leading to non compliance by policymakers. Compliance data plays a crucial role in understanding the current real-world scenario and strengthening surveillance for implementing health measures. To reduce the percentage of mortality and ultimately achieve the global goal of zero rabies deaths by 2030, the Ministry of Health and Family Welfare (MoHFW) launched a vision under the NAPRE [5]. With the focus of this program, the present study was conducted to assess the compliance of the ARV regimen managed through the intradermal route.

## MATERIALS AND METHODS

This was a cross-sectional study conducted at the Government Hospital in Gummidipoondi taluk of Thiruvallur district, Tamil Nadu, India. Data from the period of one month, specifically from April 30, 2023, to May 31, 2023, was considered for the study. The study plan was initiated in June 2023, and data collection took place in September 2023. The study was conducted after obtaining approval from the Institutional Ethics Committee (IEC) (CSP-MED/23/SEP/93/224).

The number of patients visiting the hospital for ARV ranges from 6 to 10 per day, indicating that it is an endemic area for dog bites. The Government Hospital in Gummidipoondi provides free intradermal rabies vaccine for animal bite cases treated at the hospital. After receiving approval, details were collected from the hospital's ARV register.

### Inclusion criteria:

1. All animal bite cases attending the hospital for ARV aged between 2 years and 80 years.
2. Patients of both genders seeking treatment at the hospital for ARV.
3. Category-II bite (minor scratches or abrasions without bleeding, nibbling of uncovered skin) and III bite (contaminated mucous membrane with saliva, such as licks, single or multiple transdermal bites or scratches, licks on broken skin) [5].

### Exclusion criteria:

1. Category-I bite.
2. Patients who have received pre-exposure prophylaxis.
3. Cases of re-exposure [5].

The vaccine is administered for bites from dogs, cats, rats, monkeys, and pigs. According to the Updated Thai Red Cross Schedule, 0.1 mL of the vaccine is given in 2 shots on days 0, 3, 7, and 28, administered intradermally on both deltoids [5].

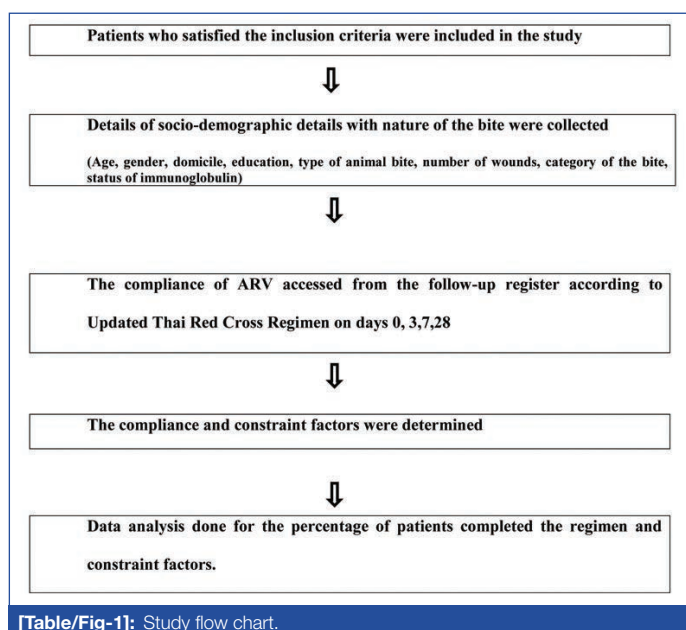
**Sample size:** Based on previous studies, with a prevalence (P) of 42.8% adherence to ARV and a 10% non response rate, the sample size was calculated for this study using the formula

$$N=4pq/d^2$$

where n=desired sample size, P (prevalence) of 42.8, q (100-p)=57.2, and a precision of 10. The sample size calculated for this study was 108 [6].

After initial wound management such as washing the wound in the hospital with running water and soap for 15 minutes, irrespective of prior cleaning, the purified lyophilised rabies antigen derived from the Rabies virus (Abhayrab) vaccine was used for intradermal injection. Following the first dose, patients were advised to return for the next three doses, with manually written dosage dates provided on paper to ensure adherence. Category-II patients received the intradermal vaccine as per the schedule. For Category-III patients, in addition to local treatment, immediate protection was provided through RIG as passive immunisation, which is highly recommended for Category-III bites [7]. Category-III patients received the rabies vaccine along with immunoglobulin (Premi-RAB: Enzyme-refined Equine Immunoglobulin 1500 IU/5 mL). The dose of immunoglobulin is 40 IU/kg body weight of the patient, administered within 24 hours, preferably by deep intramuscular injection up to the seventh day after the first dose of ARV. Both categories also received tetanus prophylaxis, with one dose of 0.5 mL of Td (Tetanus-Diphtheria) administered intramuscularly in the upper outer gluteal region. Children who had received less than three doses of the vaccine, had been more than 10 years since the last dose, or had a vaccine status of more than five years with a severe wound, received the Td vaccine. Data for the study were collected from the case proforma. Compliance with ARV was evaluated using the follow-up register. A patient is considered compliant if they complete the full ARV schedule. In cases of non adherence, the reasons for

non-adherence were identified through interviews with the patient/guardian conducted by telephone, with the details recorded in the register [Table/Fig-1].



## STATISTICAL ANALYSIS

The data was collected and coded in Microsoft Excel version 2010, and it was analysed using Statistical Package for Social Sciences (SPSS) software version 20.0. The socio-demographic variables and the compliance results were presented in the form of tables, figures, and percentages. The Chi-square test was used to determine the significance of association, with the p-value set at <0.05.

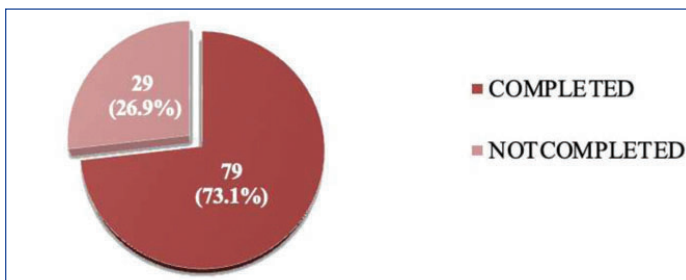
## RESULTS

Among the 108 victims, the majority were males 64 (59.3%), and the age group less than or equal to 45 accounted for 75 (69.4%) individuals with a mean age of 31.2±17.6 years. The urban area covered the most cases at 59 (54.6%), with dogs being the predominant animal at 95 (88%). Other animal bites included in the study were from rats, pigs, cats, and monkeys. Most victims experienced a single bite 89 (82.4%), categorised as Category-II in 103 (95.4%) cases, and the majority were educated with 64 (59.3%) having received some level of education [Table/Fig-2]. The compliance rate in this study was found to be 79 (73.1%) [Table/Fig-3]. Regarding compliance with ARV based on demographic profile, adherence was higher in the age group less than 45 at 55 (73.3%), male gender at 49 (76.6%), and slightly more rural individuals completed the course at 37 (75.5%). Compliance rates for other animal bites were also higher, likely due to the lower number of bites from these animals at 10 (76.9%). Compliance rates for multiple bites showed a higher percentage compared to single bites at 17 (89.5%). Adherence for Category-III bites was 5 (100%). School-goers had a higher compliance rate at 26 (83.9%). The relationship between demographic profile and ARV completion is presented in [Table/Fig-4]. However, the p-value was not statistically significant for all demographic profiles.

The compliance rate for the 2<sup>nd</sup> dose was 104 (96.3%), for the 3<sup>rd</sup> dose was 93 (86.1%), and for the 4<sup>th</sup> dose was 86 (79.6%) [Table/Fig-5]. Regarding dose delays, a total of 12 patients experienced delays. One patient was delayed by one day for the 2<sup>nd</sup> dose. For the 3<sup>rd</sup> dose, one patient was delayed by one day, and for the 7<sup>th</sup> day, out of five patients, two were delayed by two days and three were delayed by one day. On the 28<sup>th</sup> day, all six patients were delayed by one day [Table/Fig-6]. There was a decrease in the completion rate for subsequent doses, especially for the 7<sup>th</sup> and 28<sup>th</sup> day vaccine schedule, as indicated by the data. Out of the 29

Parameters	n (%)
<b>Age (years)</b>	
<45	75 (69.4)
>45	33 (30.6)
<b>Gender</b>	
Male	64 (59.3)
Female	44 (40.7)
<b>Domicile</b>	
Rural	49 (45.4)
Urban	59 (54.6)
<b>Type of animal</b>	
Dog	95 (88)
Others	13 (12)
<b>Number of wound</b>	
Single	89 (82.4)
Multiple	19 (17.6)
<b>Category of bite</b>	
Category-II	103 (95.4)
Category-III	5 (4.6)
<b>Education</b>	
Illiterates	13 (12)
Literates	64 (59.3)
School goers	31 (28.7)

[Table/Fig-2]: Demographic and other parameters.



[Table/Fig-3]: Compliance of ARV regimen.

Demographic details	Course	Completed N (%)	Not completed N (%)	Total	P-value	95% CI
Age	≤45	55 (73.3)	20 (26.7)	75	0.948	(0.410-2.591)
	>45	24 (72.7)	9 (27.3)	33		
Gender	Male	49 (76.6)	15 (23.4)	64	0.334	(0.646-3.597)
	Female	30 (68.2)	14 (31.8)	44		
Domicile	Rural	37 (75.5)	12 (24.5)	49	0.614	(0.528-2.952)
	Urban	42 (71.2)	17 (28.8)	59		
Animal	Dog	69 (72.6)	26 (27.4)	95	0.743	(0.203-3.123)
	Others	10 (76.9)	3 (23.1)	13		
Number of wound	Single	62 (69.7)	27 (30.3)	89	0.077	(0.058-1.252)
	Multiple	17 (89.5)	2 (10.5)	19		
Category	Cat II	74 (71.8)	29 (28.2)	103	0.165	(0.637-0.811)
	Cat III	5 (100)	0	5		
Education	Illiterates	10 (76.9)	3 (23.1)	13	0.216	-
	Literates	43 (67.2)	21 (32.8)	64		
	School goers	26 (83.9)	5 (16.1)	31		

[Table/Fig-4]: ARV adherence with respect to age, gender, domicile, type of animal, wound nature, category of bite and education standards.

patients who did not complete the schedule, information on the limiting factors for non adherence was collected from the follow-up register. The main obstacles were related to travel costs, hospital timings (outpatient hours), distance from the residential place, loss of wages, and some patients also missed the due dates that were

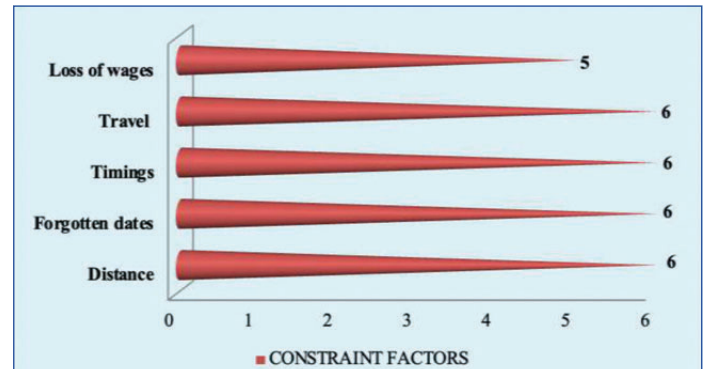
Dose	3 <sup>rd</sup> day		7 <sup>th</sup> day		28 <sup>th</sup> day	
	Received N (%)	Not received N (%)	Received N (%)	Not received N (%)	Received N (%)	Not received N (%)
No. of patients	104 (96.3%)	4 (3.7%)	93 (86.1%)	15 (13.9%)	86 (79.6%)	22 (20.4%)

[Table/Fig-5]: Vaccine compliance on scheduled dates.

Dose	3	7	28
Total no. of patients delayed	1	5	6
Delay in days	1	2 (2 Patients) 1 (3 Patients)	1

[Table/Fig-6]: Days delayed by patients for respective doses.

manually provided by the staff nurses for complete vaccination [Table/Fig-7].



[Table/Fig-7]: Constraint factors.

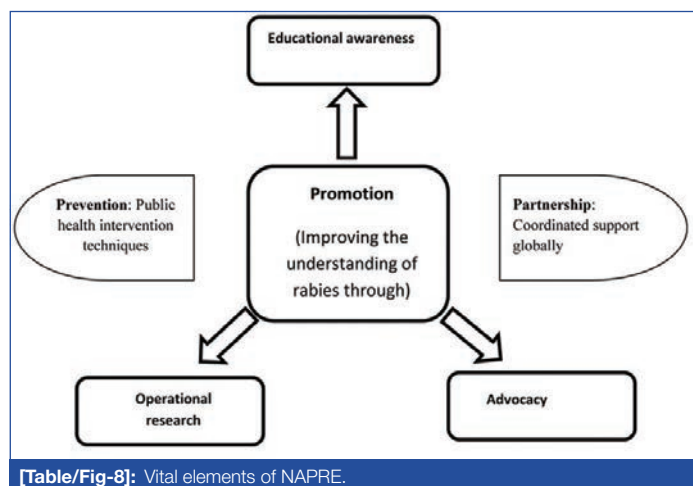
## DISCUSSION

The compliance rate of this study was found to be 73.1%. In India, under the Ministry of Health and Family Welfare (MoHFW) of India, the National Centre for Disease Control is working towards the global initiative to eliminate rabies by 2030. The program recommends a completing the vaccination course regardless of the animal's status. Currently, there are no antiviral medications or immunomodulators available for the complete cure of rabies. Therefore, a complete course of ARV is mandatory for preventing this fatal disease.

Recent advancements, such as research on the use of monoclonal antibodies like Docaravimab and Miromavimab in combination with Essen or the updated Thai Red Cross Vaccine regimen, as conducted by Manna A et al., to assess their safety in Category-III patients, have proven to be safe and effective in rabies prophylaxis [8]. The development of small molecule inhibitors and immunostimulatory substances is emerging in the modern era. In-vitro models, such as si-RNA-based studies, also demonstrate promising results [9]. Effective management is essential, especially in light of these recent developments.

In a study conducted by Kulkarni P et al., with a sample size of 100 patients, the compliance rate was 14.6% [10]. Similarly, in a study by Titoria R and Gupta G, also with a sample size of 100, the compliance rate was 43% [6]. This current study, with a compliance rate of 73.1%, showed a significantly higher level of compliance compared to the previous studies. On the other hand, in a study conducted by Wadde SK et al., involving 7892 patients, the compliance rate was 58.19% [11]. Additionally, in a study by Gudegowda KS et al., with 2815 patients, the compliance rate was 79.6%, with constraint factors including forgetting dates and distance from the hospital [12]. Similarly, in a study by Panda M and Kapoor R, constraint factors included residence far from the rabies clinic, forgetfulness, fear of loss of wages, and ill advice from relatives and friends, which are almost identical to the constraints identified in this study, emphasising the need for targeted action [13]. The analysis of this study indicates that India is making progress towards its target.

Prevention, promotion, and partnership are the three key principles of the NAPRE [2]. Prevention aims to improve accessibility and affordability through the implementation of cost-effective public health measures for all individuals. Promotion plays a crucial role in the elimination process, involving advocacy, and educational awareness to enhance understanding of rabies, as highlighted in this study. Partnership involves coordinated support for anti-rabies efforts, engaging the community, urban and rural civil society, government, private sectors, and international partners [Table/Fig-8].



[Table/Fig-8]: Vital elements of NAPRE.

### Limitation(s)

Since rabies is endemic throughout India, this study could have been conducted at multiple centres to enhance the understanding of compliance. The vaccination status of non compliant patients, including whether they received the vaccine from other medical centers or became defaulters, was not known.

### CONCLUSION(S)

The compliance rate in this study was found to be 73.1%, with major constraints for non compliance being forgotten dates, distance, travel, and timing. The results of this study emphasise the need to encourage animal bite patients not only to receive the vaccine but also to adhere to the full vaccination course and address the constraint factors. Political will, community participation, operational research, sustained funds for logistics, and intersectoral

coordination are the five pillars of the NAPRE. With research as a major focus, this study was conducted with the aim of supporting and collaborating towards a rabies-free India by 2030. The study concludes that the compliance obtained enables further steps in a multisectoral approach to achieve a 100% compliance rate and eliminate the disease.

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