APCRI Journal
Volume 27, Issue 2- 2025, Pg. No. 11-15
Peer Reviewed & Open Access Journal

Research Article

Post-Exposure Adverse Outcomes of ERIG in Category 3 Animal Bite Cases – A Record-Based Descriptive Cross-Sectional Study

Shravan Ambadkar[1], Charuhas Akre[2], Uday Narlawar[3], Suchitra Sharma[4], Aman Singh[5]

[1,5]Junior Resident, [2]Associate Professor, [3]Professor & Head, [4]Senior Resident, Department of Community Medicine, Government Medical College, Nagpur, Maharashtra, India
DOI: https://doi.org/10.24321/0973.5038.202512

I N F O

Corresponding Author:
Ambadkar Shravan, Department of Community Medicine, Government Medical College and Hospital, Nagpur, Maharashtra, India
E-mail Id:
ambadkarshravan@gmail.com
Orcid Id:
https://orcid.org/0009-0002-9168-7161
How to cite this article:
Ambadkar S , Akre C, Narlawar U, Sharma S, Singh A. Post-Exposure Adverse Outcomes of ERIG in Category 3 Animal Bite Cases – A Record-Based Descriptive Cross-Sectional Study. APCRI J. 2025; 27(2): 11-15 .

Date of Submission: 2025-10-06
Date of Acceptance: 2025-12-10

A B S T R A C T

Background: Rabies is a fatal zoonotic disease, and Category 3 animal bites require immediate post-exposure prophylaxis (PEP), including the administration of rabies immunoglobulin (RIG). Equine rabies immunoglobulin (ERIG) is widely used in resource-limited settings due to its cost-effectiveness. However, concerns remain regarding its safety profile.

Objectives: To determine the prevalence and clinical range of adverse effects that occur after ERIG administration in Category 3 animal bite cases.

Methods: Using medical records of patients who received ERIG as part of PEP for Category 3 animal bites at Anti-Rabies Vaccine OPD in a tertiary care centre of Central India from June 1, 2024, to May 31, 2025, a record-based cross-sectional descriptive analysis was conducted. Applying Microsoft Excel software version 16.97 (25051114), information on demographics, bite characteristics, ERIG administration, and adverse events was extracted and evaluated.

Results: Among a total of 3492 cases, 3048 were Category 3 animal bite cases, out of which 124 (4.03%) developed a sensitivity reaction following the test dose of ERIG during the observation period. Of the 124 patients who developed sensitivity, 123 required only symptomatic management, while only 1 patient required admission.

Conclusion: ERIG is generally safe, with a low rate of mostly mild reactions. Its benefits in rabies prevention outweigh the risks. Careful monitoring ensures its safe use in public health settings.

Keywords: Equine Rabies Immunoglobulin, ERIG, Category 3 Animal Bites, Adverse Reactions, Post-Exposure Prophylaxis

Introduction

Nearly one-third of instances of rabies, a deadly but avoidable viral zoonosis, occur in India, where it is estimated to cause 59,000 deaths annually worldwide [1,2]. Single or multiple transdermal bites, scratches, or licks on broken skin are classified as category 3 exposures, requiring prompt post-exposure prophylaxis (PEP), which involves the administration of the rabies vaccine and rabies immunoglobulin (RIG) injection.[1]

Because it is less expensive than human rabies immunoglobulin (HRIG), equine rabies immunoglobulin (ERIG) is the preferred choice in settings with limited resources.[1,3] Though historically, using ERIG has been associated with hypersensitivity reactions that vary from mild urticaria to catastrophic anaphylaxis.[4-6] Its safety profile must be continuously assessed to maintain public trust in its use.[7]

The purpose of this study was to determine the prevalence and clinical range of adverse effects that occur after ERIG administration in Category 3 animal bite cases at a tertiary care centre.

Materials and Methods

This record-based, descriptive, cross-sectional study was conducted at the Anti-Rabies Vaccine (ARV) Outpatient Department of a tertiary care centre in Central India to evaluate adverse outcomes following Equine Rabies Immunoglobulin (ERIG) administration in Category 3 animal bite cases. All patients who reported Category 3 animal bites and who received ERIG as part of post-exposure prophylaxis (PEP) were included during the 12-month data collection period, which occurred between June 1, 2024, and May 31, 2025. Patients without ERIG or with insufficient therapy information were not included. At the study site, ERIG is administered as per national guidelines. A 0.02 mL intradermal test dose is given on the volar forearm using a tuberculin syringe, ensuring a small wheal. Patients are observed for 30 minutes for any local (itching, erythema, wheal enlargement) or systemic (rash, dyspnoea, hypotension) hypersensitivity reactions. Sociodemographic information (age, sex, residence), bite features (kind of animal), post-exposure prophylaxis information (ERIG dosage, history of prior immunization, tetanus toxoid suggested), and adverse events after ERIG administration were all taken from patient records. Mild adverse effects included local urticaria, itching, erythema, injection site pain, and nausea. Moderate side effects included systemic symptoms such as fever, malaise, and a widespread rash that required medical attention. Severe side effects included severe hypersensitivity reactions, such as anaphylaxis, that required immediate medical attention. Descriptive statistics were used to examine the data, which were then imported into Microsoft Excel 2019 and presented as frequencies, percentages, and proportions. The Institutional Ethics Committee granted ethical approval for the study [Approval No. 3534(a)], and patients' IDs were anonymized to maintain patient privacy.

Results

In Table 1, a total of 3492 animal bite cases were studied. Age distribution revealed that the mean age was approximately 31 years, with the 15-29-year-old age group having the highest proportion (32.3%), followed by those aged 45 and above (25.3%), those aged 30-44 (21.6%), and those younger than 15 years (20.8%). Males (67.7%) were more than females (32.3%). The majority of cases (84%) came from urban areas, with only 16% from rural locations. Dogs were responsible for 84.8% of the exposures, followed by cats (10.3%), monkeys (2.2%), and other animals (2.8%). The vast majority of bites have been categorised as Category III (87.3%), with Category II and I accounting for 12.4% and 0.3%, respectively. Of those individuals who were given RIG, 95.9% had no adverse responses, with 4.07% experiencing minor reactions. Only 15.2% claimed a history of past rabies immunisation, whereas 84.8% had never been vaccinated, indicating a huge susceptible population.

Table 1. Distribution of Socio-Demographic and Exposure Characteristics among Animal Bite Victims (N=3492)

Variable	Category	Frequency (n)	Percentage (%)
Age group (years)	<15	727	20.82%
	15–29	1126	32.25%
	30–44	754	21.59%
	≥45	885	25.34%
Sex	Male	2363	67.67%
	Female	1129	32.33%
Residence	Urban	2933	83.99%
	Rural	559	16.01%

ISSN: 0973-5038
DOI: https://doi.org/10.24321/0973.5038.202512

Variable	Category	Frequency (n)	Percentage (%)
Type of animal	Dog	2961	84.79%
	Cat	359	10.28%
	Monkey	76	2.18%
	Others (Wild pig, etc.)	96	2.75%
Category of animal bite	Category I	10	0.29%
	Category II	434	12.43%
	Category III	3048	87.28%
RIG administration outcome	No (Adverse reaction)	2924	95.93%
	Yes (Adverse reaction)	124	4.07%
Previous rabies immunization status	No	2960	84.77%
	Yes	532	15.23%

The findings in Table 2 suggested that the majority of the 124 patients who experienced adverse reactions after ERIG treatment were mild (95.16%), followed by moderate reactions (4.03%), with only one case (0.81%) classified as severe. The chi-square test (χ^2=213.5, df=2, p<0.001) demonstrated that the distribution of adverse reaction types was highly skewed, with a statistically significant predominance of mild reactions over moderate or severe ones. This implies that significant adverse effects were extremely uncommon, and most reactions were modest and treatable, reaffirming the safety profile of ERIG in the management of Category III animal bite patients.

In Table 3, among the 3048 Category III bite patients treated with ERIG, 124 (4.07%) had adverse effects, the majority of which were mild. Stratified analysis revealed no significant differences across age groups (<15, 15-29, 30-44, ≥45; χ^2=4.68, p=0.197), gender (male vs female; χ^2=0.54, p=0.461), residence (urban vs rural; χ^2=0.68, p=0.409), animal type (dog, cat, monkey, others; χ^2=4.8, p=0.187), or previous rabies immunisation status (yes vs no; χ^2=2.42, p=0.120). These findings suggest that adverse reactions to ERIG are uncommon and do not vary significantly by demographic or exposure variables, highlighting the overall safety and acceptability of ERIG in Category III animal bite cases.

Table 2.Distribution of Adverse Reactions Following ERIG Administration (N=124)

Adverse Reaction Type	Frequency (n)	Percentage (%)	Chi-square (df = 2)	p-value
Mild	118	95.16%	213.5	<0.001
Moderate	5	4.03%		
Severe	1	0.81%		
Total adverse events	124	100%		

Table 3. Subgroup Analysis of Adverse Reactions Following ERIG Administration in Category III Bite Cases (N=3048)

Variables	Adverse Reaction	No Adverse Reaction	Total	Chi-square (df)	p-value
Age Groups					
<15	25	619	644	4.68 (3)	0.197
15–29	46	902	948		
30–44	30	633	663		
≥45	23	770	793		
Sex					
Male	81	2014	2095	0.54 (1)	0.461
Female	43	910	953		

ISSN: 0973-5038
DOI: https://doi.org/10.24321/0973.5038.202512

Variables	Adverse Reaction	No Adverse Reaction	Total	Chi-square (df)	p-value
Residence					
Urban	107	2428	2535	0.68 (1)	0.409
Rural	17	496	513		
Type of animal					
Dog	99	2498	2597	4.8 (3)	0.187
Cat	15	298	313		
Monkey	6	67	73		
Others (Cows, rabbits, mongooses, bats, pigs, horses, etc.)	4	61	65		
Previous Immunization					
No	112	2480	2592	2.42 (1)	0.120
Yes	12	444	456		

Discussion

The adverse effects of administering Equine Rabies Immunoglobulin (ERIG) in Category III animal bite cases were evaluated in this record-based descriptive cross-sectional study. Only 4.07% of individuals experienced adverse reactions from 3,048 Category III exposures, and the great majority (95.2%) had mild reactions, with only one severe reaction documented. Importantly, subgroup analysis supported the broad safety profile of ERIG across a variety of subgroups by showing no statistically significant correlation between bad outcomes and exposure or demographic factors such as age, sex, residence, animal type, or prior rabies vaccination.

Our results align with those of previous studies from both India and other countries, which similarly reported that significant reactions were extremely uncommon, and most of the ERIG-related adverse effects were moderate[7]. The majority of ERIG reactions are restricted to local urticaria or pruritus, with serum-sickness-like illness occurring seldom and case series from India. Purified equine F(ab')2 fragments were used in previous extensive multicenter assessments conducted in Thailand and the Philippines[8,9]. These evaluations revealed an outstanding safety profile, with no reduction of vaccine-induced immunity and minor systemic responses. Thus, our results are consistent with ERIG safety data from around the world.

Monoclonal antibody (mAb) products, such as TwinRab and Rabishield, have been introduced as ERIG substitutes in India in recent years. According to post-marketing surveillance studies and phase-4 multicentric trials, these products are safe, well-tolerated, and free of responses similar to serum sickness [10]. Additionally, comparative evaluations highlight their consistent neutralizing antibody titres and non-immunosuppressive characteristics. However, in many public health settings, where ERIG is still the most popular option, cost and availability concerns continue to be limiting factors.

The WHO's stance that ERIG is safe and should be administered as warranted without undue concern for adverse outcomes is supported by the extremely low prevalence of severe adverse outcomes in our study. A key aspect of rabies elimination programmes is ensuring that RIG, whether equine or monoclonal, is available, as stated in the WHO's most recent rabies biologics guidance and Indian opinion[11].

In high-burden countries like India, ERIG is still a cost-effective and practical choice for widespread use, despite its equestrian origin. Risks can be further reduced by using appropriate delivery methods, following test dosage recommendations, and having emergency care on hand.

This study's strength lies in its thorough, record-based evaluation from a tertiary care centre setting and its large sample size. The use of routine records, which can underreport minor self-limiting occurrences, and the incapacity to document late-onset problems, including serum sickness, that appear after discharge, are some of the limitations. More reliable estimates could be obtained from prospective pharmacovigilance research.

There is still a major vulnerable pool, and the importance of prompt PEP with ERIG cannot be highlighted enough, as more than 85% of bite victims in our study had never

ISSN: 0973-5038
DOI: https://doi.org/10.24321/0973.5038.202512

received prior rabies vaccination. Both patients and physicians should be reassured by fewer adverse events, which will promote greater adoption and adherence.

Conclusion

Equine Rabies Immunoglobulin (ERIG) is safe and well-tolerated in Category III animal bite cases, according to this record-based study. Adverse responses occurred in only 4.07% of patients, with the great majority being mild and manageable. The lack of a significant correlation between bad outcomes and exposure or demographic variables highlights the safety and wide-ranging application of ERIG across patient categories. These results provide reassurance to doctors and policymakers, as India's rabies control efforts still rely on ERIG. However, they also emphasise the need for ongoing surveillance and the gradual adoption of monoclonal antibody substitutes as they become more widely available.

Acknowledgments

The authors gratefully acknowledge the cooperation of the staff of the Anti-Rabies Vaccine (ARV) Outpatient Department in the Tertiary Care Centre of Central India for their assistance in facilitating access to patient records. We also thank the Institutional Ethics Committee for their guidance and approval of the study. Special thanks are extended to colleagues who provided valuable inputs during data collection and analysis.

Conflict of Interest: None

Sources of Funding: None

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process: None

References

1. World Health Organization. Rabies vaccines: WHO position paper. Geneva: WHO; latest update. [Pubmed]
2. Goel K, Sen A, Satapathy P, Kumar P, Aggarwal AK, Sah R, Padhi BK. Emergence of rabies among vaccinated humans in India: a public health concern. The Lancet Regional Health-Southeast Asia. 2023 Feb 1;9. [Google Scholar] [Pubmed]
3. Lang J, Simanjuntak GH, Soerjosembodo S, Koesharyono C. Suppressant effect of human or equine rabies immunoglobulins on the immunogenicity of post-exposure rabies vaccination under the 2-1-1 regimen: a field trial in Indonesia. MAS054 Clinical Investigator Group. Bulletin of the World Health Organization. 1998;76(5):491. [Google Scholar] [Pubmed]
4. Wilde H, Chutivongse S. Equine rabies immune globulin: a product with an undeserved poor reputation. [Google Scholar] [Pubmed]
5. Shah M, Taneja V, Khosla P. Serum sickness like reaction postequine rabies immunoglobulins. J Assoc Phys India. 2023 Dec 1;71:95-7. [Google Scholar] [Pubmed]
6. Ashe S, Routray D, Behera TR. Serum sickness following equine rabies immunoglobulin administration-a case study. [Google Scholar]
7. Krishnan J, Kanchana BM, Ushakumari A, Suresh R, Abraham S. Adverse events following equine rabies immunoglobulin administration among category 3 animal bite exposures. Preventive Medicine: Research & Reviews. 2025 May 1;2(3):111-3. [Google Scholar]
8. Quiambao BP, Dy-Tioco HZ, Dizon RM, Crisostomo ME, Teuwen DE. Rabies post-exposure prophylaxis with purified equine rabies immunoglobulin: one-year follow-up of patients with laboratory-confirmed category III rabies exposure in the Philippines. Vaccine. 2009 Nov 27;27(51):7162-6. [Google Scholar] [Pubmed]
9. Jatuporn Sirikun MD, Ploypailin Ratanachinakorn MD, Somphon Roeksomtawin MD. Safety and Non-Suppressive Effect of a Purified F (ab') 2 Equine Rabies Immunoglobulin in WHO Category III Rabies Exposed Patients. Journal of the Medical Association of Thailand. 2018:563. [Google Scholar]
10. Shankaraiah RH, Masthi NR, Poornima MK, Kiruffi V, Sowmyashree S, Dutta T, Mahajan M, Desai S. Safety Evaluation of the Novel Cocktail of Monoclonal Antibodies for Postexposure Prophylaxis in Category III Animal Exposures. Journal of Global Infectious Diseases. 2024 Oct 1;16(4):140-4. [Google Scholar] [Pubmed]
11. Krishna NS, Thangaraj JW, Devika S, Sasi A, Egambaram S, Rani DS, Khan SA, Delli A, Srivastava AK, Mishra A, Shrinivasa B. Availability of anti-rabies vaccine and rabies immunoglobulin in Indian health facilities: a nationwide cross-sectional health facility survey. The Lancet Regional Health-Southeast Asia. 2025 Jul 1;38. [Google Scholar] [Pubmed]