

Title: ASSESSMENT OF HYPERSENSITIVITY REACTIONS FOLLOWING EQUINE ANTI RABIES IMMUNOGLOBULIN INOCULATION AMONG CATEGORY-III BITE CASES ATTENDING RURAL TERTIARY CARE INSTITUTE IN HARYANA

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Keywords Hypersensitivity reactions, Equine anti rabies immunoglobulin, category-III bite cases

Abstract Rabies is a fatal and vaccine-preventable viral disease transmitted by the saliva of the wild or rabid animal. Timely and correct post exposure prophylaxis for the exposed victims is necessary to prevent rabies. The anti-rabies serum/Rabies Immunoglobulin is an essential component of rabies post exposure treatment as it provides passive immunity. Equine rabies immunoglobulin has been available commercially in developing countries and instances of anaphylaxis or serum sickness caused by it varies. A few studies conducted to report hypersensitivity reactions following Equine anti rabies immunoglobulin test dose inoculation, hence this study was planned

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Aims and objective: 1. To find out hypersensitivity reactions following equine anti-rabies immunoglobulin test dose inoculation

2. To find association of status of hypersensitivity reactions with post-exposure anti-rabies vaccination status

Methodology: Record based cross-sectional study was conducted among category-III bite cases attending, the anti-rabies clinic during **1st March, 2016** to **28th Feb 2017**. Category-I and II bite cases, Category-III bite cases with incomplete records and those who had not given their consent

for equine anti rabies immunoglobulin inoculation were excluded from the study. Data was entered in Microsoft excel 2010 and analyzed using Statistical Package for the Social Sciences software version 17.0.

Observations: 210 participants had given consent for equine anti rabies immunoglobulin test dose inoculation. Among them 126 (60%) were males and 84 (40%) were females and *majority of cases 174 (83%) belonged to rural area* and in majority of cases *188 (89.5%) source of exposure was dog*. Average delay in reporting to anti-rabies clinic was 1.04 ± 1.27 days. All the category-III bite cases tested for hypersensitivity reactions and 94 (45%) cases reported to have hypersensitivity reactions.

Conclusion and recommendations: Mild hypersensitivity reactions were observed following Equine anti rabies immunoglobulin test dose inoculation and a large proportion had not completed anti-rabies post-exposure immuno-prophylaxis. There is a need to strengthen Information, Education and Communication based programme in the community and regular health education sessions in anti-rabies clinics to create awareness for completion of anti-rabies post-exposure immuno-prophylaxis to control the disease.

Original Article

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ABSTRACT:

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Observations: 210 participants had given consent for equine anti rabies immunoglobulin test dose inoculation. Among them 126 (60%) were males and 84 (40%) were females and majority of cases (79.5%) belonged to rural area and majority of cases 186 (89.2%) source of exposure was dog. Average delay in reporting to anti-rabies clinic was 1.04 ± 1.27 days. All the category-III bite cases tested for hypersensitivity reactions and 94 (45%) cases reported to have hypersensitivity reactions.

Conclusion and recommendations: Mild hypersensitivity reactions were observed following Equine anti rabies immunoglobulin test dose inoculation and a large proportion had not completed anti-rabies post-exposure immuno-prophylaxis. There is a need to strengthen Information, Education and Communication based programs in the community and regular health education sessions in anti-rabies clinics to create awareness for completion of anti-rabies post-exposure immuno-prophylaxis to control the disease.

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INTRODUCTION:

Rabies is a fatal but vaccine-preventable viral disease which occurs in more than 150 countries and territories. It is a neglected zoonotic disease caused by the rabies virus of the *Lyssa virus* genus within the family *Rhabdoviridae* and poses a potential threat to >3.3 billion people worldwide¹. The virus is transmitted by the saliva of the wild or rabid animal and generally enters the body via infiltration of virus laden saliva from a rabid animal to other animals / humans through bites, scratches, licks on broken skin, and mucous membranes^{2,3}. As per World Health Organization's in South East Asia Region more than 1.4 billion people are at risk of infection due to large human and animal interaction leads to more exposure among them, thereby it continues to be a major public health problem throughout the region⁴.

India is also a rabies endemic country and an estimated 17.4 million animal bites occur annually which accounts to an incidence of 1.7% among exposed population⁵. Each year 21000 - 24000 deaths occur in South East Asia Region due to rabies and India accounts for

estimated 18000 - 20000 human rabies deaths per year. However it is estimated that in the absence of post exposure prophylaxis, about 3, 27,000 people would die from rabies in Asia and Africa each year and more than 15 million people worldwide receive anti rabies post exposure prophylaxis every year to prevent this disease. Timely and correct post exposure prophylaxis (PEP) for the exposed victims is necessary to prevent rabies^{6,7}.

The anti-rabies serum/Rabies Immunoglobulin (RIG) is an essential component of rabies post exposure treatment as it provides passive immunity in the form of ready-made anti-rabies antibodies, before it is physiologically possible for the victim to begin producing his/her own antibodies following anti-rabies vaccination. Anti-rabies serum or RIG has the property of binding with the rabies virus, thereby resulting in neutralization and thus loss of infectivity of the virus and hence it is most logical to infiltrate RIG locally at the site of exposure. Equine rabies immunoglobulin (ERIG) has been available commercially in India⁸. It has been claimed that ERIG cause serum sickness in 15-46% of recipients^{9,10}; in general, however in this regard,

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reports have not differentiated between ERS and the newer, purified ERIG preparations. In contrast, HRIG is well tolerated, and instances of anaphylaxis or serum sickness caused by it are virtually unknown¹¹. HRIG is, however, expensive and not generally affordable in developing countries, where canine rabies remains a serious public health problem¹². There are a few studies conducted to report hypersensitivity reactions following Equine anti rabies immunoglobulin inoculation among category-III bite cases in this region. Hence this study was conducted to reveal types of hypersensitivity reactions which occurred following Equine anti rabies immunoglobulin inoculation among category-III bite cases.

Aims and objective:

1. To find out hypersensitivity reactions following equine anti-rabies immunoglobulin test dose inoculation
2. To find association of status of hypersensitivity reactions with post-exposure anti-rabies vaccination status among category-III cases

METHODOLOGY:

Study setting: Immunization cum antirabies clinic, Bhagat Phool Singh Government Medical College for Women Kharpur Kalan, Sonapat.

Study design: Record based cross-sectional study.

Study population and sample size: All of the category-III bite cases.

Study variables: Age, sex, locality, any delay in reporting to clinic, wound toileting with soap and water, tetanus toxoid vaccination, adherence to required schedule of antirabies vaccination and any hypersensitivity reaction noted after 30 minutes of test dose of equine anti rabies immunoglobulin.

Inclusion criteria: All of the category-III bite cases as per National guidelines on rabies prophylaxis¹³, attended anti-rabies clinic during the study period i.e. 1st March, 2016 to 28th Feb 2017.

Exclusion criteria: Category-I and II bite cases, Category-III bite cases with incomplete records and those who had not given their consent for equine anti rabies immunoglobulin inoculation.

All the category-III exposed cases offered the equine anti rabies immunoglobulin and anti-rabies vaccine free of cost. Data entry was done by trained personnel in Microsoft excel version 2010 and supervised by the researcher to ensure the correctness of secondary data.

Ethical issue: Being a record based anonymous study there was no any ethical issue.

Statistical analysis: Analyzed using Statistical Package for the Social Sciences (SPSS; Windows version 17.0) software. Percentages & proportions was applied for

drawing inferences and obtaining conclusion.

Results: In this present record based study secondary data was used. A total of 3841 cases reported to the anti-rabies clinic during study period. Out of 261 exposed cases of category-III; 210 participants had given consent for equine anti rabies immunoglobulin inoculation / hypersensitivity test dose. Among them 126 (60%) study participants were males and 84 (40%) were females (male/female ratio 1.5). The age distribution of the cases ranged from 2 year to 95 years, with a mean age of 40.78 ± 21.68 years (median 40 years). Among them 30 (14%) of of category-III exposed cases belonged to below 15 years age group while 43 (21.5%) cases were 60 years years and above. Majority of cases 174 (83%) belonged to rural area and in majority of cases 188 (89.5%) source of exposure was dog. Average delay in reporting to anti-rabies clinic was 1.04 ± 1.27 days. All the category-III bite cases were tested for hypersensitivity reactions and 94 (45%) cases reported to have hypersensitivity reactions.

Table-1:

Profile of category-III bite cases attending anti-rabies clinic during study period

Attribute		Study participants N(%)
		18(230)
Sex	Male	126(60)
	Female	84(40)
Locality	Rural	174(83)
	Urban	36(17)
Source of exposure	Dog bite	188(89.5)
	Monkey bite	21(10)
	Cat bite	1(0.5)
Site of exposure	Lower limb	153(73)
	Upper limb	31(24)
	Chest and above	6(3)
Wound toileting with soap and water	Done after exposure	84(40)
	Not done for exposure	126(60)
Tetanus toxoid	Already taken from outside	17(8)
	Given in anti-rabies clinic	173(82)

Figure in parenthesis indicate percentages

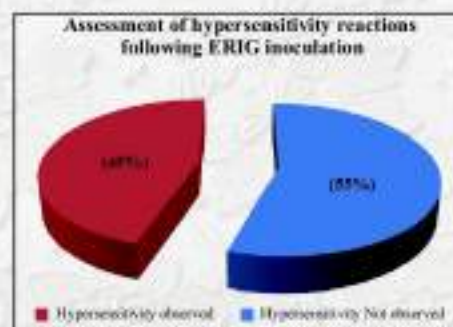


Table-2:
Types of hypersensitivity reactions observed following Equine anti rabies immune-globulin test dose inoculation among category-III bite cases

Attribute	Study participants N(%) (n=94)
Localized swelling	39(41.5)
Dizziness	22(23.4)
Localized swelling and redness	11(11.7)
Headache	8(8.5)
Vertigo and nausea	7(7.4)
Vertigo and dizziness	5(5.3)
Localized swelling, redness and itching	1(1.0)
Localized swelling and dizziness	1(1.0)

Figure in parenthesis indicate percentages

Localized swelling was most common hypersensitivity reaction observed among 39 (41.5%) study subjects followed by dizziness among 22 (23.4%) and most common hypersensitivity reaction in combination was observed as localized swelling and redness i.e. among 11 (11.7%) study participants.

Table-4:
Association of status of hypersensitivity reactions with post-exposure anti-rabies vaccination status

Hypersensitivity reactions	Anti-rabies vaccination status N(%) (n=210)		
	Not completed	Completed	Total
Observed	60(63.8)	54(36.2)	114(100)
Not observed	53(45.7)	63(54.3)	116(100)
Total	113(53.8)	97(46.2)	210(100)

DF=1, p-value=0.05

Discussion: This study assessed the socio-demographic profile, status of post-exposure anti-rabies vaccination and assessment of hypersensitivity reactions observed among animal exposed category-III cases following equine anti-rabies immunoglobulin test dose inoculation attending the rural tertiary care centre. The study also explored the relationship among status of hypersensitivity reactions with post-exposure anti-rabies vaccination status. All the 210 cases of category-III received the equine anti rabies immunoglobulin and anti-rabies vaccine free of cost. It was observed that the victims were largely males 126 (60%) (male/female ratio was 1.5:1) and the major source 188 (89.5%) of exposure was dog. Similar observations were found in various studies that males affected were more^{39,40} and dog bites caused maximum morbidity^{39,40}. The overall male/female ratio of animal bite victims among Asian countries was 1.6:1⁴¹. However in a WHO survey conducted in India male/female ratio was found to be 2.19:1⁴². Likely this is related to occupational or behavioral factors or due to outdoor activity that place them in greater contact with the animal vector i.e. dog. It was found that before coming to anti-rabies clinic 84 (40%) animal bite cases done wound toileting with soap and water or water alone after exposure. Slightly lower value was observed in a study conducted by Shelke SC et al in which wound toileting practices after exposure

were observed among 34% cases³⁹. In a multi-centric study carried out in Mumbai revealed that wound toileting practices were higher (58.5%) than that of our study³⁹. These practices varied from one region to another because of cultural practices and awareness regarding wound toileting. Although WHO recommendations included that immediate wound toileting is to be done after exposure to animal⁴³.

In the present study it was found that hypersensitivity reactions were observed following Equine anti rabies immunoglobulin test dose inoculation among 94 (45%) of cases, while 116 (55%) cases have no any reaction. **Only mild hypersensitivity reactions were observed and none of the case anti-rabies immunoglobulin was contraindicated.** It has been claimed that Equine antirabies serum (ERS) and equine rabies immunoglobulin (ERIG) cause serum sickness in 15-46% of recipients⁴⁴.

The study revealed that no serious systemic side effects were observed following Equine anti rabies immunoglobulin test dose inoculation and only local side effects like localized swelling, localized redness, dizziness. Similar findings were demonstrated in a study conducted by Behara T et al in 2011 which showed no serious systemic side effects but local side effects like local pain, indurations due to ERIG⁴⁵.

The present study found that 97 (46.2%) cases completed their anti rabies post exposure immunoprophylaxis (PEP) schedule while 113 (53.8%) cases had not completed the recommended schedule. It might be due to awareness regarding severity of disease still lacking in the community. Also the institution being in deep rural area accessibility would be another reason for non compliance to adherence to post exposure prophylaxis regimen.

The study explored that among cases having observed hypersensitivity reactions, 34 (36.2%) had completed the post exposure anti-rabies immune-prophylaxis while 60 (63.8%) cases had not. However, among cases having no observed hypersensitivity reactions 63 (54.3%) had completed their anti-rabies post exposure immunoprophylaxis and 53 (45.7%) had not completed. The association of hypersensitivity reactions and anti rabies post exposure immunoprophylaxis status was found to be statistically significant (p value < 0.05). It might be due to the fact that after having hypersensitivity reaction they might be scared of or lack of awareness regarding fatality of the disease and hence not completed their post-exposure immunoprophylaxis.

Conclusion and recommendations: The study reports mild hypersensitivity reactions were observed following Equine anti rabies immunoglobulin test dose inoculation and a large proportion had not completed

anti-rabies post-exposure immuno-prophylaxis. There is a need to strengthen Information, Education and Communication (IEC) based programme in the community and regular health education sessions in Immunization cum anti-rabies clinic to create awareness for completion of anti-rabies post-exposure immuno-prophylaxis to control the disease.

Limitation of the study: As the study was conducted only at one rural tertiary health care facility and sample size was very small. Also follow-up had not been done for any delayed hypersensitivity reaction after equine antirabies immunoglobulins inoculation to beneficiaries hence results could not be generalized.

Conflict of interest: Nil declared

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ANNOUNCEMENT

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