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TO ESTIMATE THE SEROCONVERSION RATE AMONG VACCINE DROPOUT OF RABIES IN DISTRICT AMRITSAR

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Abstract

Background: - Rabies is a vaccine preventable deadly disease. There is a lack of organized surveillance system on animal bite victims to ensure completion of full course of post-exposure prophylaxis. **Objective:** - To estimate seroconversion rate among vaccine dropout of Rabies and assessment of sociodemographic profile of Rabies dropout cases. **Methods:** - This prospective study was conducted among patients who attended Guru Nanak Dev Hospital, Government Medical College, Amritsar, in Anti-Rabies Clinic between the periods ranging from July, 2023 to December, 2024. Study population comprised of vaccine drop out cases bitten by animals known to cause Rabies. A 5 mL of whole blood was extracted in a plain vacutainer from suspected patients and enzyme-linked immunosorbent assay (ELISA) was performed. **Results:** - Total of 93 samples were collected out of which 72 were vaccine dropouts and 21 were related to Pre-Exposure Prophylaxis. Rate of Seroconversion increased with the number of doses. **Conclusion:** - Rate of Seroconversion is directly proportional to number of completed doses. Proper dosage at scheduled time is utmost important to achieve high seroconversion rates. High/Sufficient Seroconversion was observed in all cases after complete vaccination schedule.

Keywords: Rabies, Seroconversion, Vaccine dropout.

INTRODUCTION

Rabies, caused by a lyssavirus, is a viral zoonosis that affects people in many parts of the world, especially those in low-income countries. Contact with animals, especially dogs, is the main source of human infections. Humans may present with the disease only after a long period of exposure. Nearly half of rabies cases occur in children <15 years old.[1] The WHO leads the "United against Rabies" Campaign to progress toward "Zero human deaths from dog-mediated rabies by 2030." Still, it is an endemic lethal disease, even after 100 years of the invention of its vaccine by Louis Pasteur and Emile Roux in 1885.[2]

Rabies is the 10th biggest cause of death due to infectious diseases worldwide. Every year, more than 15 million people worldwide receive post-exposure vaccination.[3] Rabies is a major public health problem in most of the developing world.[4] The disease is prevalent in all continents except Antarctica. More than 95% of human deaths caused by rabies occur in Africa and Asia. An estimated 45% of all deaths from rabies occur in South East Asia. The situation is especially pronounced in India, which reports about 18,000 to 20,000 cases of rabies a year and accounts for about 36% deaths worldwide.[5] The Indian subcontinent comprises Afghanistan, Bangladesh, Bhutan, India, Nepal, the Maldives, Myanmar, Pakistan and Sri Lanka. In all of these countries, except for the Maldives, rabies is endemic. An estimated 59,000 people die from rabies each year; 45% of these deaths occur in the Indian subcontinent and approximately 33% of these occur in India.[6]

On the account of various economic and political factors, multiple cultural, religious and social practices, multiples myths associated with rabies, and lack of accurate data, even though economic and effective control measures are available; the disease has not been brought under control.[7,8,10] Although effective preventive and control measures such as Animal Birth Control, prophylactic vaccination of Animals, pre-exposure prophylaxis, and post-exposure prophylaxis of

human are available in rural and urban communities of Punjab, lack of epidemiological data poses threat to its effective implementation. The success of any preventive and control measure requires a strong epidemiological surveillance mechanism. There is no published data on Sero-surveillance of dropout cases from Punjab. With this background the present study was conducted to estimate seroconversion rate among vaccine dropout of Rabies and assessment of sociodemographic profile of Rabies dropout cases.

MATERIAL & METHODS

This prospective study was conducted among patients who attended Guru Nanak Dev Hospital, Government Medical College, Amritsar, in Anti-Rabies Clinic between the periods ranging from July, 2023 to December, 2024. Study population comprised of vaccine drop out cases bitten by animals known to cause Rabies.

Operational definition of dropout of Anti-rabies vaccine (ARV) for the purpose of present study – Any individual who has started taking ARV after animal bite but has either discontinued the vaccination or there has been gap/delay as per the prescribed schedule, has been considered to be a dropout, as discussed below: -

- *In case of intradermal (i.d) schedule*

  - gap/delay of 3 or more days during the first 3 doses of (i.d) schedule, or
  - gap of >7 days between 3rd and 4th dose,

- *In case of intramuscular (i.m) schedule*

  - gap/delay ≥ 3 days gap in first 4 doses of (i.m) schedule.
  - gap of >7 days between 4th and 5th dose

During the course of the present study, A 5 mL of whole blood was extracted in a plain vacutainer from suspected patients and Quantitative enzyme-linked immunosorbent assay (ELISA) was performed.

We collected various information regarding their social demographical and clinical profile like age, gender, occupation, nativity (urban/rural), literacy, type (stray/pet), type of exposure (Category/severity of wound), Type of first aid treatment taken before reporting to hospital, route and schedule of ARV, immunoglobulin doses, wound washing, local instillation, etc. were analysed. Further seroconversion as per the WHO recommendations was studied. The results thus obtained are as per the observations and results tabulated and explained with the bar chart/pie chart etc.

Platelia Rabies-II, IgG antibody detection kit is an immune-enzymatic technique for the detection of rabies virus anti-glycoprotein antibodies. It is a semiquantitative kit. A microplate is coated with rabies glycoprotein extracted from the inactivated and purified virus membrane. The amounts of anti-Rabies antibodies present in the samples were detected as per kit protocols.

Inclusion criteria:

1. Patients with history of animal bite.
2. Patients who have not followed the standard vaccination schedule as prescribed by NRCP (National Rabies Control Program).
3. Patients who give written informed consent.

Exclusion criteria:

1. Patients who have followed the vaccination regime.
2. Patients who do not give written informed consent.
3. Patients bitten by animals not known to cause Rabies.

Study period: -July 2023 to December 2024.

PRINCIPLE OF THE PLATELIA ™ RABIES II ASSAY

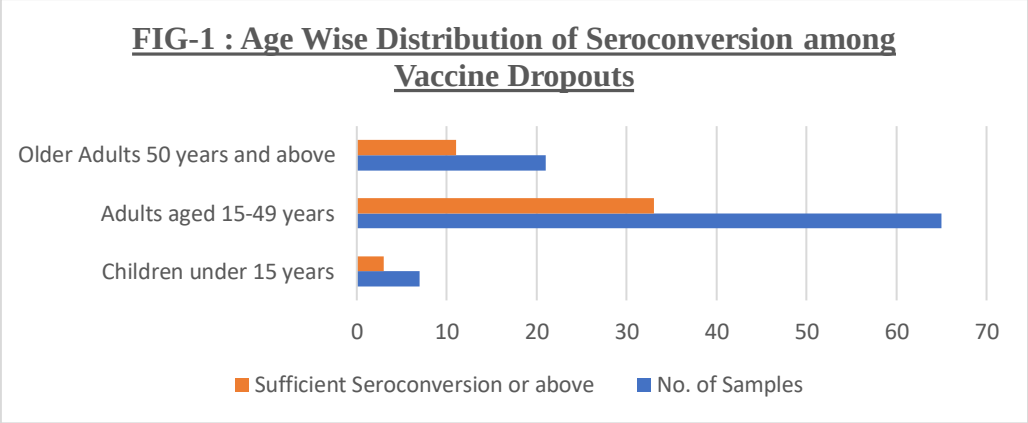
PLATELIA™ RABIES II is an immuno-enzymatic technique for the detection of rabies virus anti- glycoprotein antibodies. This assay can be carried out on the human serum or plasma sample. The test is based on the use of a solid phase enzyme immunoassay technique referred to as an indirect ELISA. A microplate is coated with rabies glycoprotein extracted from the inactivated and purified virus membrane. The enzymatic conjugate consists of a protein A from Staphylococcus aureus coupled with peroxidase. Positive controls, calibrated against WHO standard, allow the qualitative or quantitative determination of anti-rabies antibody titre in the serum or plasma.

The presence of immune complex is demonstrated by the addition of a solution containing a peroxidase substrate and a chromogen, initiating a color development reaction. The optical density reading obtained with a spectrophotometer set at 450-620 nm is proportional to the amount of anti-rabies antibodies present in the samples.

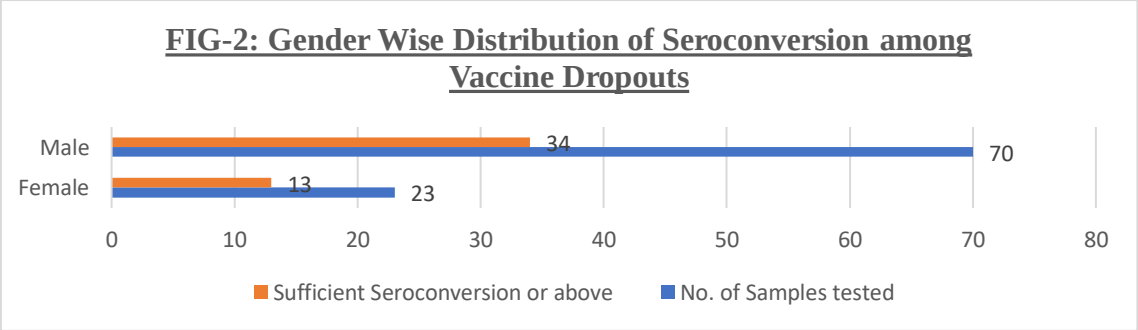
RESULTS

The present prospective study was conducted in the Department of Microbiology, Government Medical College, Amritsar from July, 2023 to December, 2024. A total of 93 samples (10 samples in AY 2023 and 83 samples in AY 2024) of vaccine dropouts were obtained in the Anti Rabies Clinic in Guru Nanak Dev Hospital attached to Government Medical College, Amritsar. The samples were tested for the presence of Quantitative IgG by Indirect ELISA from blood samples by Enzyme linked immunosorbent Assay (ELISA) in serum. Out of the above 93 samples, 72 were vaccine dropout and 21 were related to Pre-Exposure Prophylaxis.

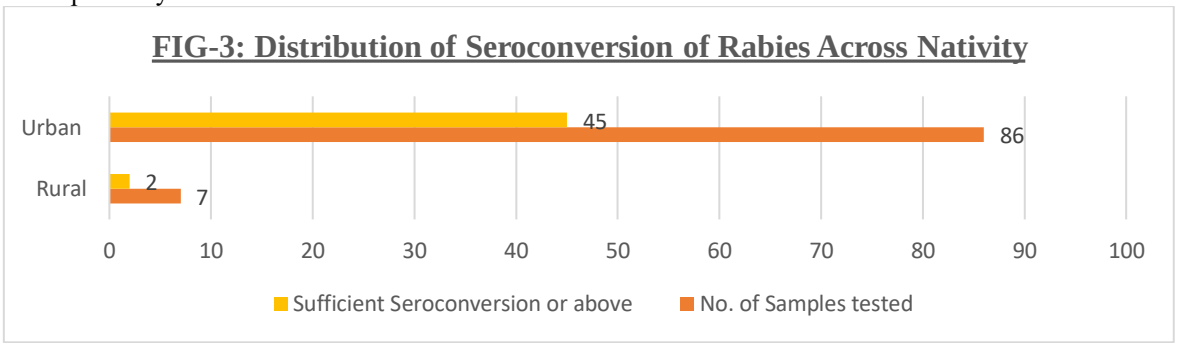
The Most common age group of animal bite victims were 15-49 years (65, 69.89 %), followed by adults above 50 years and above (21, 22.58 %) and children below 15 years (7, 7.53 %). Consequently, the Predominant Age group developing Sufficient Seroconversion or above also belongs to the individuals aged 15 years and above (33, 50.77 %).



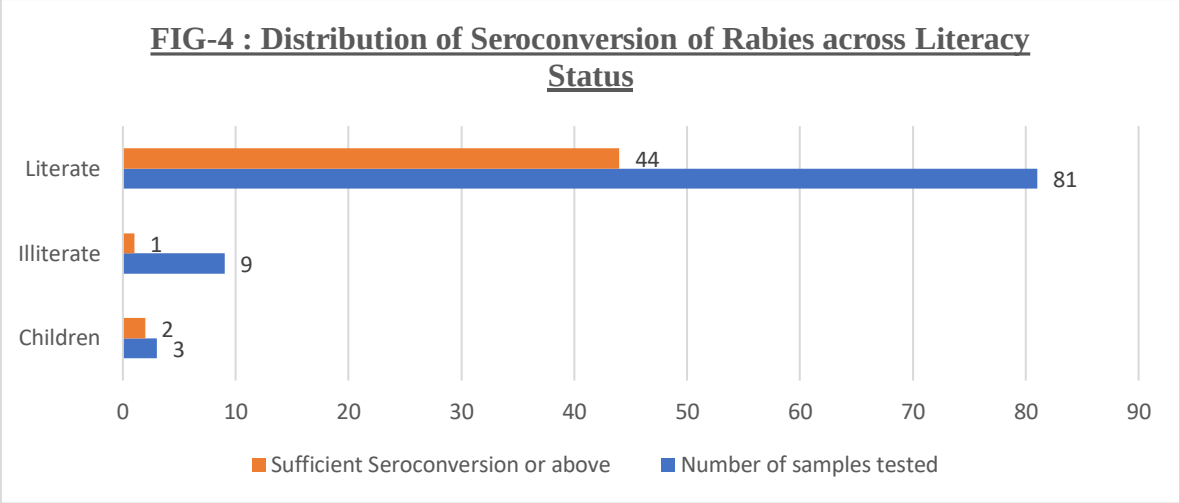
Out of the 93 vaccine dropout samples enrolled in this study, 70 were males and 23 were females. This could be explained by the involvement of males in outdoor works which increases the chances of animal bite in comparison to females. However, among these vaccine dropouts, more than half of the females (56.52%), developed IgG antibodies against Rabies.



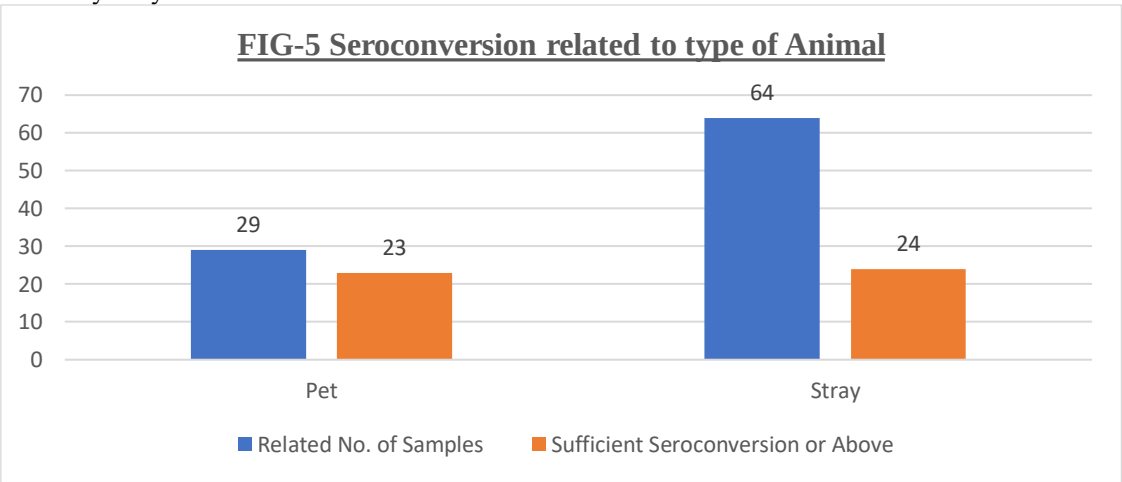
Most of the vaccine dropouts (92.47 %) enrolled in the study belonged to the urban areas, while only 7.53 % were residing in rural areas. However, among the vaccine dropouts of urban and rural areas, 52.33 % and 28.57 % of the dropouts respectively exhibited Sufficient Seroconversion or above.



Among the vaccine dropouts enrolled in this study, 87.10 % were literate, 9.68% were illiterates and 3.23 % belonged to children segment. Majority of samples belonging to children and literate vaccine dropouts exhibited sufficient seroconversion or above during the course of this study.



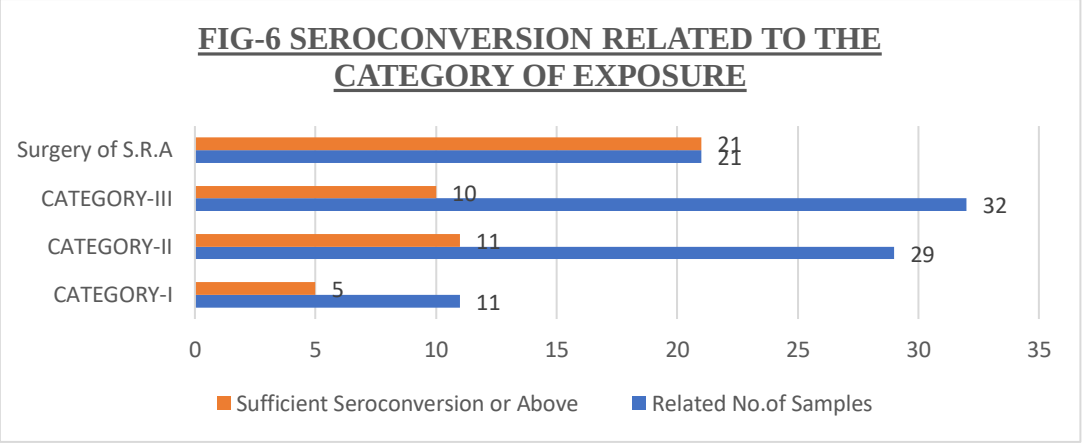
Among the vaccine dropouts tested for seroconversion of rabies, majority of them were bitten by stray dogs (68.82%), while 31.12 % of the Pet dogs contributed to biting incidences. On the contrary, 79.31 % of the vaccine dropouts bitten by pets have exhibited sufficient seroconversion or above during the course of this study, while only 37.50 % of vaccine dropouts bitten by strays have exhibited sufficient seroconversion or above.



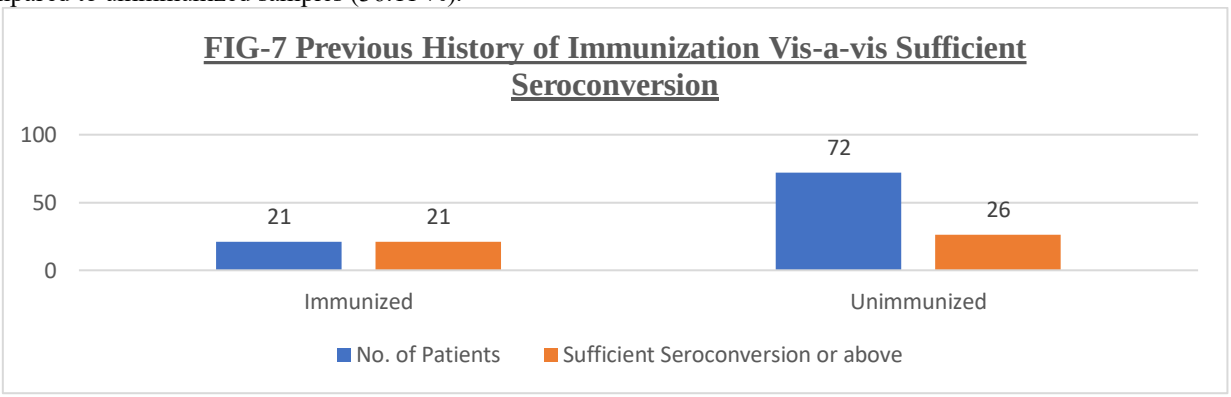
As per the 3RD Report on "Expert Consultation on Rabies" by the WHO, the following categories describe the risk of a RABV exposure according to the type of contact with the animal suspected of having rabies. The category of exposure determines the indicated PEP procedure:

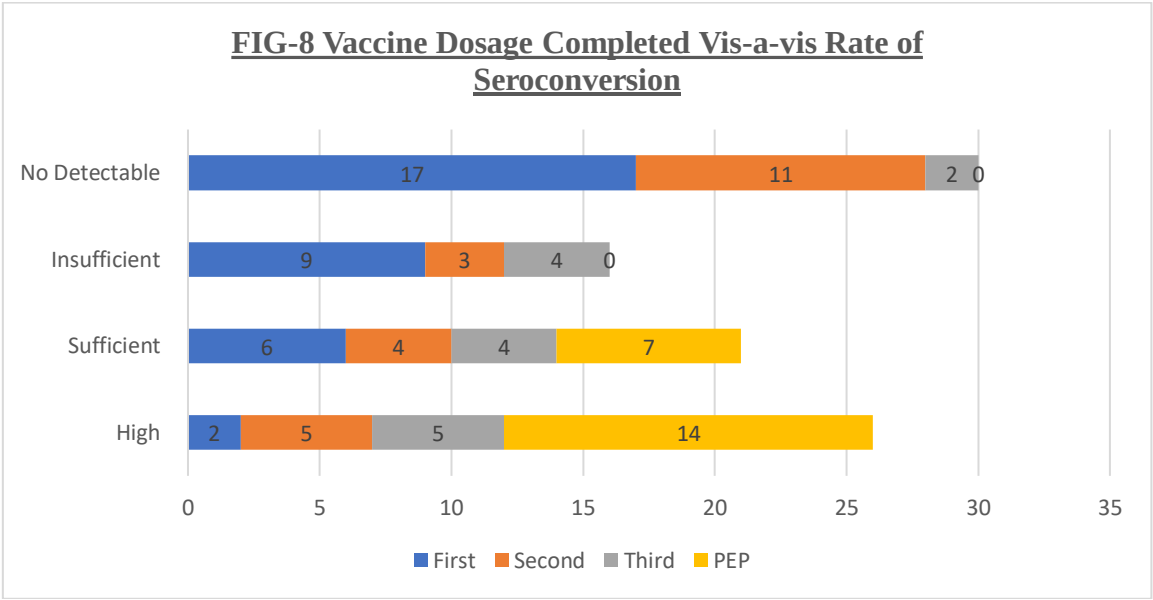
Category I	touching or feeding animals, animal licks on intact skin (no exposure);
Category II	nibbling of uncovered skin, minor scratches or abrasions without bleeding (exposure);
Category III	single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (severe exposure).

Majority of the vaccine dropouts enrolled in the study were exposed to Category-III Exposure with single or multiple bites with bleeding (34.41 %). However, 45.45 % of the vaccine dropouts exposed to Category-I exposure exhibited sufficient seroconversion or above, followed by Category-II (37.93 %) and Category-III (31.25 %). All the samples related to Pre-Exposure Prophylaxis (exposure during surgery of suspected Rabied animal) exhibited sufficient seroconversion or above.



Around 77 % vaccine dropouts were unimmunized i.e. they had no history of any immunization, while all the veterinary doctors who had performed surgeries on rabid dogs were immunized. Further it has been observed that the seroconversion sufficiency of immunized samples (Veterinary Doctors along with their students) was 100 %, as compared to unimmunized samples (36.11 %).





During the course of the study, it was observed that percentage of dropout vaccine samples having sufficient seroconversion was more for those individuals who had taken three dosages of vaccine viz. 60 % as compared to others who had completed one or two doses. The same was 100 % in case of samples who had completed Pre-Exposure Prophylaxis.

DISCUSSION

Rabies a fatal disease, caused by a lyssavirus, is a vaccine-preventable viral disease. In rabies-endemic countries, completing the full course of ARV is essential to prevent the disease. The present study was conducted to estimate seroconversion rate among vaccine dropout of Rabies and assessment of sociodemographic profile of Rabies dropout cases.

Rabies vaccine can prevent rabies if given to a person after an exposure. Recommended first-aid procedures include immediate and thorough flushing and washing of the wound for a minimum of 15 minutes with soap and water, detergent, povidone iodine or other substances of proven lethal effect on rabies virus. [9] All suspected rabies cases should be treated immediately to prevent the onset of clinical symptoms and death. Post-exposure prophylaxis (PEP) consists of wound treatment, the administration of rabies vaccines based on WHO recommendations, and if indicated, the administration of rabies immunoglobulin. Two types of vaccines to protect against rabies in humans exist - nerve tissue and cell culture vaccines.

The most common age groups bitten by animal bites were 15-49 years (69.89 %), followed by more than 50 years (22.58 %) and children of less than 15 years (7.53%). Most of the victims were males (75.27 %) with females as only 24.73 % (overall Male: Female Ratio= 3::1). This is Consistent with other studies viz. Dhaduk, et al[8], Vinodhraja et al [16]. The study done by Dhaduk, et al in the year 2015 at Jamnagar, Gujarat was regarding case profile and dropout rate of Anti Rabies Vaccination (ARV), regimens among animal bite victims in Gujarat, in which, the majority of victims were males (Male: Female Ratio= 3::1); among them children < 15 years age group (26%) & Youth 15-30 years group (28 %) were affected more as reported by similar studies [10,13, 17, 20]. This might be due to the reason that they are highly kinetic and engaged in outdoor activity without proper precaution.

In the study conducted by Vinodhraja Sellan [16] on Dropout rate of Anti Rabies Vaccination among rural and urban communities in Tamil Nadu in the year 2021: A Comparative Cross Sectional Study, the majority (61.9 %), victims were males among them, 33 % were children 0–20-year group and 37.4 % were youth 21–40-year group [16]. Similarly, the WHO National multi-centric rabies survey 2003, assessing the burden of rabies in India by APCRI reported that majority of victims (76 %) were adult men [18] and a multicentric study in India by Bhattacharya et al was conducted in the year 2008 (across six selected centres across the country viz. Delhi, Hyderabad, Raipur, Jamnagar, Koonoor and Rajahmundry and was co-ordinated by National Institute of Communicable Diseases (NICD), Delhi), also reported similarly that 72.4 % were male among them children 47.5%. [19] Likewise Shankaraiah Et al., in the year 2015 at Bengaluru found that 66.7% were males among them 21.7% were Children < 15 years. [11]. This could be explained by the involvement of males in outdoor works which increases the chances of animal bite in comparison to females.

In the present study, the number of dropout victims from urban area is 92.47 % and rural 7.53% This is similar to results of Dhaduk, et al.[8] In the study done in Gujarat 82.4 % were from urban areas and 17.6 % were from rural areas. As per an article on profile of animal bite victims attending anti- rabies clinic in a tertiary care hospital, Bengaluru by Subathra V [15] the same were 87.3 % and 12.7 % respectively.

In the present study, the literacy rate of dropout victims was observed as 87.10 % literate & 9.68 % illiterate. This is similar to the study done in Bengaluru by Subathra V [15] where the dropout rate among literate patients was 78.3 % and 21.7 % were illiterates. In a study done in North Karnataka during the year 2014 by Dr. Pavithra [21] where the dropout rate among literate patients was 80.4 % and 19.6 % were illiterates.

Regarding the type of dog (stray/pet) the victims who visited the hospital were 68.82% (victims of stray dogs) and 31.18% (victims of Pet dogs). This is similar to the study done in Bengaluru [15] by Subathra V where these ratios are 65% (stray) and pets 35%. However, this ratio is in contrast to the study in Karnataka by Dr. Pavithra R [21] where pet dogs were responsible in 60% of cases while 36.8% cases were bitten by stray dogs.

In the present study it was observed that the victims who dropped out, after the first dose were 23.53%, after second dose were 39.13% and after third dose were 60 %. In a study in Eastern India (Rural Orissa) by Sahu et al during the year 2019. [14] the dropout rate was 7.8 %, 14.4 % and 25.5 % respectively after 1st, 2nd and 3rd Dose. In the study, done by Dhaduk, et al [8] in Gujarat dropout was most commonly encountered between the third dose (Completed, by 96.3% of the total victims) and the fourth dose (Completed by 66% of total victims), while Biswas et al. [22] reported 41.2% dropout in third dose. In the study done by Vinodhraja, et al. in Tamil Nadu [16], the overall Complete coverage to full course of ARV combining urban and rural area was found to be as low as 48.8% & this was similar to findings of Shankaraiah et al., Sahu et al, & Abhay et al.in their study of compliance to ARV [11, 17, 12].

The Vaccine dropout cases coming to the hospital had exposure of Category-I wound (11.83%), category-II wound 31.18% and category III wound - 34.41%. Similar results were obtained in the study done by a study conducted in Bengaluru by Subathra V in the year 2015 [15].

Seroconversion rate of health workers dealing with rabies animals must be tested for Seroconversion from time to time & vaccinated that covered under Pre-exposure Prophylaxis.
Regarding Seroconversion sufficiency of the vaccine dropouts, it was observed that the rate increased with every dose. Thus, proper dosage at scheduled time is utmost important to achieve high seroconversion rates.

CONCLUSION

There is a need to sensitize the communities through a strong information, education and Communication programme with respect to the hazards of animal bite and its consequences, immediate reporting of dog bites, importance of proper wound care, necessity of taking anti rabies vaccination, dangers of inadequately managed animal bites wound, registration, licensing and vaccination of all domestic dogs, importance of Animal Birth Control, Anti Rabies Vaccination (ABC-AR) program and co-operating with the authorities in its implementation.
The National Action Plan for Dog medicated rabies Elimination from India by 2030 envisages to achieve Zero human deaths due to dog mediated rabies by 2030. This is proposed to be achieved through sustained, mass dog vaccination and appropriate post-exposure treatment under One Health Approach for Rabies Elimination.
The Rate of Seroconversion is directly proportional to number of completed doses as high/Sufficient Seroconversion was observed in all cases after complete vaccination schedule. Proper dosage at scheduled time is utmost important to achieve high seroconversion rates since the disease is nearly 100% fatal, however it is preventable by complete vaccination, so no change in vaccination schedule should be attempted unless recommended by NRCP.
Rabies is a vaccine preventable disease, 59000 deaths were reported annually, out of which one-third takes place in India. Major cause is not reporting and not completing the vaccination schedule. Government has launched free vaccination, mass campaigns, information, education and communication programmes for the same. There is a need for motivating people to report regarding animal bite cases and educate people to complete the vaccination schedule.

AUTHORS CONTRIBUTION

All authors contributed satisfactorily to the study.

CONFLICTS OF INTERESTS

The authors declare that they have no conflicts of interest

AUTHOR'S FUNDING

None.

REFERENCES

1. Amoako YA, El-Duah P, Sylverken AA, Owusu M, Yeboah R, Gorman R et al. Rabies is still a fatal but neglected disease: a case report. J Med Case Rep. 2021;15(1):1-6.
2. World Health Organization. Fact Sheets Rabies. Geneva: World Health Organization. Available from: https://www.who.int/news room/fact-sheets/detail/rabies
3. Subathra V, Kishore SG, Ranganath TS, Kumar A. Profile of animal bite victims attending anti-rabies clinic in a tertiary care hospital, Bengaluru. RGUHS Nat J Pub Health. 2016;1(2):62-7.
4. Zhang X, Zhu Z, Wang C. Persistence of rabies antibody 5 years after postexposure prophylaxis with vero cell antirabies vaccine and antibody response to a single booster dose. Clin Vac Immunol. 2011;18(9):1477-9.
5. Pavithra R, Viveki RG, Halappanavar AB. Socio demographic profile and management practices of animal bite cases attending anti rabies clinic in a tertiary care centre in North Karnataka. IJAR. 2015;5(1):371.
6. Rahman SA, Isloor S. Rabies on the Indian subcontinent. Revue Scientifique et Technique (International Office of Epizootics). 2018;37(2):529-42.
7. Ichhpujani RL, Bhardwaj M, Mala C and Datta KK. Rabies in India. Country Report. IN: 4th International Symposium on Rabies Control in Asia, Vietnam; March, 2001. p. 35. http://dx.doi.org/10.4103/0019-557X.195855
8. Dhaduk KM, Unadkat SV, Katharotiya PR, Mer AR, Chaudhary MC, Prajapati MM. Case profile, volume analysis, and dropout rate of anti-rabies vaccination regimens among animal bite victims in Gujarat. Ind J Pub Health. 2016;60(4):268-72.
9. WHO – Control of Neglected Tropical Diseases – Local treatment of wounds.
10. Ichhpujani RL, Mala C, Veena M, Singh J, Bhardwaj M, Bhattacharya D, et al. Epidemiology of animal bites and rabies cases in India. A multicentric study. J Commun Dis 2008;40:27 36.

11. Shankaraiah RH, Rajashekar RA, Veena V, Hanumanthaiah AN. Compliance to anti rabies vaccination in post exposure prophylaxis. Indian J Public Health 2015;59:58 60.
12. Abhay K, Rishabh KR, Sunil K, Veena R, Roy C. Factors influencing animal bite cases and practices among the cases attending the anti rabies clinic DMCH, Darbhanga (Bihar). Int J Recent Trends Sci Technol 2013;6:94 97.
13. Umarigar P, Parmar G, Patel PB, Bansal RK. Profile of animal bite cases attending urban health centres in Surat city: A cross sectional study. Natl J Community Med 2012;3:631 35.
14. Sahu DP, Preeti PS, Bhatia V, Singh AK, Singh A. Anti-Rabies vaccine compliance and knowledge of community health worker regarding animal bite management in rural area of Eastern India. Cureus. 2021;13(3):14229.
15. Subathra V, Kishore SG, Ranganath TS, Kumar A. Profile of animal bite victims attending anti-rabies clinic in a tertiary care hospital, Bengaluru. RGUHS Nat J Pub Health. 2016;1(2):62-7.
16. Sellan V, Chenchu KR, Ashokkumar V, Mani E. Dropout rate of anti-rabies vaccination among rural and urban communities in Tamil Nadu: A comparative cross-sectional study. Asian J Med Sci. 2023;14(1):65-9.
17. Sahu KK, Manar MK, Singh SK, Singh H. Epidemiological characteristics of patients attending for rabies post exposure prophylaxis at the infectious disease's hospital of Lucknow, India. J Glob Infect Dis 2015;7:30 32.
18. World Health Organization. WHO Sponsored National Multi-Centric Rabies Survey 2003: Assessing Burden of Rabies in India. APCRI. Geneva: World Health Organization. Available from: https://www.rabies.org.in/rabies/wp-content/ uploads/2009/11/whosurvey [Last accessed on 2021 Feb 22]
19. Ichhpujani RL, Mala C, Veena M, Singh J, Bhardwaj M, Bhattacharya D, et al. Epidemiology of animal bites and rabies cases in India. A multicentric study. J Commun Dis. 2008;40:27-36.
20. Shankaraiah RH, Rajashekar RA, Veena V and Hanumanthaiah AN. Compliance to anti-rabies vaccination in post-exposure prophylaxis. Indian J Public Health. 2015;59:58-60. https://doi.org/10.4103/0019-557X.15286
21. Pavithra R, Viveki RG, Halappanavar AB. Socio demographic profile and management practices of animal bite cases attending anti rabies clinic in a tertiary care centre in North Karnataka. IJAR. 2015;5(1):371.
22. Biswas M, Kar K, Satpathy DM, Giri PP. A study on drop out among animal bite cases (provoked versus unprovoked) attending the ARV clinic SCB Medical College, Cuttack. APCRI J 2014; 15:21 23.