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EPIDEMIOLOGY AND TREND OF RABIES POST EXPOSURE PROPHYLAXIS AT ANTI RABIES CLINIC OF A TERTIARY CARE HOSPITAL IN INDIA

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Background and Objectives *Effective prevention of rabies is possible by vaccination following a rabid animal bite. Objectives of this study was to describe demographics, circumstances of bite and the trend of vaccination over last three years (January 2019–November 2021) in an anti-rabies clinic of a tertiary care hospital.*
Materials and Methods *This was an observational study of prospective design. All animal bite victims who attended the anti rabies clinic (ARC) of the study institution during the study period were invited to participate in the study. Data was collected using a structured schedule on first visit and at 28th day to check for on time compliance to vaccination schedule. On time completion was defined as taking all vaccine doses on due dates. Distribution of variables was shown by frequencies and percentages. Indicators were recorded for three consecutive years. Year wise indicators were compared by chi-square test.*
Results *Data was collected for 293 victims. Median age of bite victims was 41.8 years (range 3–78 years) while 58.7 % respondents were below 45 years of age; 71.3 % victims were male. 82.3 % bites were by dogs; 38 % victims had multiple bites. Post-exposure prophylaxis (PEP) with anti-rabies vaccine (ARV) was initiated within 72 hours for 80 % victims and it was completed on time for 66.2 % victims. Three years trend for PEP indicators did not show a statistically significant difference.*
Conclusion *On time PEP schedule completion was fairly high at the studied ARC. Health seeking for PEP following animal bite was not affected by the corona virus pandemic*
Keywords: *Rabies, Rabies vaccine, Post-exposure prophylaxis, Viralzoonoses*

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1. Introduction

Rabies is a viral zoonotic disease that causes progressive and fatal inflammation of the brain and spinal cord. Once clinical signs appear, rabies is almost always fatal. At the same time rabies is entirely preventable. Effective vaccines and immunoglobulins are available to prevent death from rabies. Nevertheless, rabies still continues to kill 59,000 humans every year. Of these cases, approximately 99 % are acquired from the bite of an infected dog. A burden of this disease is disproportionately higher for the poorest and marginalised population, living in Africa and Asia. In many countries human rabies cases do not occur. They still may report imported cases due to increasing dog ownership and incur costs for maintaining disease freedom or surveillance of endemic rabies transmission in wildlife [1, 2]. A global plan for rabies control and elimination has been agreed upon by Food and Agriculture Organisation of the United Nations (FAO), World Organisation for animal health (OIE) and World Health Organisation (WHO) in **Zero by 30: The Global strategic plan to end human deaths from dog-mediated rabies by 2030.** A key component to achieve this goal is to improve access to post-exposure prophylaxis (PEP) to animal bite victims [3].

The coronavirus pandemic has overwhelmed health systems as a result of which routine immunization services were disrupted [4–6]. The present situation compromised vaccine supply chains, and bite victims were less likely to seek healthcare due to intermittent lockdowns and fear of contacting COVID. (4) Incomplete vaccination with anti-rabies vaccine (ARV) in PEP has been observed due to multiple injections and repeated office visits [7, 8]. In the presence of COVID travel restrictions and non-COVID immunization being given lower priority, ARV compliance needed to be explored. Given the crucial importance of PEP in controlling fatal human rabies, a study was undertaken at the anti-rabies clinic (ARC) of a tertiary care hospital with the following objectives:

1. Describing demographics and circumstances of bite among animal bite victims, attending ARC for PEP.
2. Proportion of beneficiaries, completing PEP on time.
3. Trend of PEP service at the selected ARC over last three years (January 2019-November 2020).

2. Materials and Methods

This is an observational study of prospective design, which adhered to the STROBE guidelines. All ani-

mal bite victims who attended ARC of Medical College Kolkata to begin or continue ARV for PEP from January 2019 to November 2021 were eligible to participate in this study.

2.1. PEP protocol at the ARC

ARV has no contraindication. Cell culture anti rabies vaccine is administered following either Thai Red Cross regimen – 0.1ml two site intradermal (ID) vaccines on day 0,3,7 and 28 or Essen regimen- 0.5 ml one site intramuscular (IM) vaccines on day 0,3,7,14,28. Essen regimen is given to only those who are immunocompromised or if IM schedule has already started somewhere else. For Category III bites if a victim presents within 72 hours of bite, half of the calculated dose of rabies immunoglobulin (RIG) is infiltrated around the wound and rest of the amount is given as IM injection.

2.2. Participant recruitment, data collection and outcome measure

This study is compliant with the bioethics policy as stated in the Declaration of Helsinki. The protocol was approved by institutional ethics committee of Medical College Kolkata with ref no.MC/KOL/IEC/NON-SPON/1107/10/18. Informed consent to participate was provided by all participants. Data elements did not include any personal identifier, so anonymity of participants was ensured.

All the animal bite victims who attended the ARC during the study period were invited to participate in the study. Exclusion criteria were patient's refusal to participate or grave injuries, requiring immediate critical care. Data was collected from January 2019 to November 2021, using a structured schedule, which included variables like age, sex, working status, living arrangement (demographic variables), variables, related to circumstance of bite and biting animal, measures, taken following bite and whether previously received ARV. Data was collected on first visit and at 28th day to check for on time compliance to the vaccination schedule. On time completion was defined as taking all vaccine doses on due dates. WHO category of bites was used for defining Category II and III bite [9]. Age was recorded in completed years according to valid government issued identity. Education level was categorized as less than primary (did not enroll in school or did not complete education up to fourth standard), primary (completed education up to fourth standard), secondary (completed education up to tenth standard) and tertiary (any level of education beyond tenth standard including diploma/degree in pure/applied/professional/vocational streams). Indicators were compared for three consecutive years. Microsoft Excel 2010 was used for data entry and calculation. Year wise indicators were compared by χ^2 test for association of variables. Distribution of variables was shown by frequencies and percentages. Median was calculated for participant's age.

3. Results

The response rate at the ARC was 98 %. Data was available for 293 respondents over three years. Median age of the victims was 41.8 years and only 6.8 % of victims were aged lower than 15 years. Maximum number of respondents was in the age category of 30–44 years. More than half of the patients (57 %) were educated up to the primary level or lower. There was male preponderance and 21.2 % victims were homeless, living in camps, shelter or on street (Table 1).

Table 1

Distribution of animal bite victims according to their demographic characteristics (n=293)

Variables	Frequency (%)
Age (in years)	
<15	20 (6.8)
15–29	54 (18.4)
30–44	98 (33.5)
45–59	56 (19.1)
≥60	65 (22.2)
Median age (range)	41.8 (3–78)
Sex	
Male	209 (71.3)
Female	84 (28.7)
Education	
Primary not completed	63 (21.5)
Primary	104 (35.5)
Secondary	74 (25.3)
Tertiary	52 (18.7)
Working Status	
Working	178 (60.8)
Not working/homemaker	115 (39.2)
Living arrangement	
Home	231 (78.8)
Camps/Shelter/Street	62 (21.2)

Table 2 shows findings, related to circumstances, category of bite and extent of PEP with ARV. It was observed 71 % victims had category III bite and dogs were the commonest biting animal (82.3 %). More than half of the bites were from pet animals yet most animals were either unvaccinated or of unknown vaccination status. Almost two-thirds of the bites occurred during daytime. The majority (92 %) of vaccines were given by intradermal route, following Thai Red Cross regime. PEP with rabies immunoglobulin (RIG) was received by 39.6 % of category III bite victims. PEP was started with ARV within 72 hours of bite for 80 % victims and 66.2 % victims completed PEP with ARV on-time.

Table 3 shows the comparison of indicators for current and past two years. Number of beneficiaries steadily increased from 2019 to 2020. Apparently the proportion of timely completion of PEP schedule increased over the years. However this difference was not statistically significant. The proportion of category III bites decreased in 2020 but again increased in 2021. Initiation of ARV schedule within 72 hours of bite remained fairly constant over the years. By chi-square tests, none of the indicators significantly varied over the years.

Table 2

Distribution of animal bite victims according to circumstances, category of bite and post-exposure prophylaxis (n=293)

Variables	Frequency (%)
Species of biting animal	
Dog	241 (82.3)
Cat	36 (12.2)
Other animals	7 (2.4)
Animal not identified	9 (3.1)
Type of animal	
Pet	169 (57.7)
Stray/Wild	124 (42.3)
WHO Category of bite	
Category II (scratches)	85 (29.0)
Category III (transdermal bites)	208 (71.0)
Number of bites	
Single	182 (62.1)
Multiple	111 (37.9)
Anatomical site of bite	
Head & neck	42 (14.3)
Trunk	30 (10.2)
Limbs	221 (75.4)
Vaccination status of animal	
Unknown	152 (51.9)
Vaccinated	74 (25.3)
Not vaccinated	67 (22.9)
Time of bite	
Day	179 (61.1)
Night	114 (38.9)
Duration from bite to ARV0 dose (in hours)	
<24	194 (66.2)
24–72	58 (19.8)
>72	41 (14.0)
Immediate Wound washing	
Done	232 (79.2)
Not done	61 (20.8)
Post-exposure RIG	
Given	116 (39.6)
Not given	177 (60.4)
Past H/O ARV	
Pre-exposure prophylaxis	9 (3.1)
Post-exposure prophylaxis	18 (6.1)
ARV naive	266 (90.8)
Type of ARV schedule	
Intradermal	271 (92.5)
Intramuscular	22 (7.5)
Timely completion of ARV	
Yes	194 (66.2)
No	99 (33.8)

Table 3

Trend of anti rabies vaccination at the anti rabies clinic of Medical College, Kolkata from 2019–2020

Indicators	Year			
	2019 (n=83) Frequency (%)	2020 (n=98) Frequency (%)	2021 (n=112) Frequency (%)	P-value
Category III bites	59 (71.1)	67 (68.4)	82 (73.2)	0.7
Timely completion of vaccination schedule	48 (57.8)	65 (66.3)	81 (72.3)	0.1
Immediate wound washing	66 (79.5)	79 (80.6)	87 (77.7)	0.8
ARV0 dose within 72 hours of animal bite	74 (89.2)	86 (87.8)	92 (82.1)	0.3

4. Discussion

This study reports the high proportion of timely initiation of PEP with ARV among animal bite victims. Almost two-third of PEP beneficiaries completed their schedule on time. Despite of the onslaught of COVID pandemic, ARC indicators remained constant in 2020–2021 when compared to pre-COVID times (2019).

Demographics of the bite victims enrolled in this study were compared with that of ARC attendees from similar studies, conducted in India. Comparator studies reported the similar level of male preponderance among bite victims as in the present study [10–12]. However age groups were dissimilar as other studies report higher proportion of victims of age <15 years and much lower proportion among senior citizens. WHO too reports 40 % of cases among <15 years of age [9]. Such differences can be attributed to background demography unique to each region and closure of schools as a response to the pandemic, reducing opportunity of human-canine contact among <15 years age group. The compulsion to stay indoors might be responsible for higher proportion of bites by pet animals in our study as it was much lower (38.1 %) in the study, conducted at Mandya, Karnataka [12]. Dogs were reported in literature as a primary source of human rabies [13, 14]. The majority of animal bite victims in this study presented with dog bites; notably there were also 12 % victims of cat scratch or bite. Ra-

bies is included under neglected tropical diseases (NTD). As already discussed rabies elimination is a global target along with other NTDs [3]. According to the 2nd International meeting report of Pan African Rabies Control Network (PARACON), neglected tropical diseases are a proxy for disadvantage [15]. In the present study nearly one-fifth of the victims were homeless. The Mandya study too reports 48 % victims, having monthly income of < 65USD [12]

Prompt PEP following severe exposures is 100 % effective in preventing rabies. However, delay in seeking PEP, improper wound care, unnoticed wounds, direct nerve inoculation, and lack of patient compliance with vaccination schedules, are known factors, which contribute to PEP failure and subsequent death [16]. In the present study >60 % victims started PEP early and completed on time, about 80 % victims undertook immediate wound care; it is of concern that the risk of disease still remains for 20–40 % victims. Compliance to 4-dose intradermal rabies vaccine (IDRV) and the proportion of Category III bites in the Mandya study was at somewhat higher at 71.8 % and 82.4 % (66.2 % and 71 % in the present study) [12]. The variable for ARV completion in the present study was more strictly defined as completion of schedule on due dates, the possibly lower value was obtained. In the latest position paper on rabies WHO recommends shorted ARV schedules and reserving RIG for severe category III exposures [9]. RIG coverage in the present study and that from Mandya was low but much higher than the global estimate of <2 % [17]. The new recommendations will likely improve rabies PEP related indicators. Despite of disruption of routine immunization (RI) services in India from 2020 onwards, which is yet to recover to pre COVID levels, the current study reports ARV service to be maintained at the pre COVID level [18]. A study, done in USA, reports reduction in preventive and elective procedures in the beginning of the COVID pandemic, contrary to which the total number of beneficiaries at the ARC in the present study increased compared to pre COVID times[19].

Limitations of the study. Present study was conducted at a single hospital, so it did not provide information on those animal bite victims who did not come for PEP, which is a limitation of this study.

Prospects for further research. The studies have reported non-receipt of PEP among more than half of animal bite victims in South East Asian countries [20]. Community knowledge on rabies, the protection, offered by PEP, and behavior change communication, related to health seeking among bite victims, will help in realizing the 'zero by thirty' target.

5. Conclusion

1. The animal bite victim demography is changing with a decline in bites among less than 15 years of age and increase among the elderly population.

2. Dogs, especially pet dogs were the commonest biting animal. More than two-thirds of the bites were category III bites. Initiation of post-exposure prophylaxis, following animal bite was early, within a day of bite, for 66 % of bite-victims. More than 90 % of ARV injections were given by ID route, which is more cost-effective. There was fairly good compliance to existing vaccination schedule.

3. Unlike other vaccines, health seeking for rabies post exposure prophylaxis with anti-rabies vaccine was not affected by the coronavirus pandemic, as the turn-out for vaccination was similar to pre-pandemic times.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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