

## A CLINICAL STUDY ON RABIES

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### Summary

*Rabies is a fatal but easily preventable disease became one of the major public health problems in Bangladesh. This study carried out in Infectious Disease Hospital (IDH) Dhaka, Bangladesh to see different clinical presentation of rabies, to evaluate the incubation period and the interval between appearance of symptoms and time of death of the patients. All the clinically diagnosed cases of rabies referred to IDH were included in the study. The data was collected from the patient attendant by using a structured questionnaire. Among 101 patients- most of the cases (85.2%) came from rural area and children less than 15 years were major victims (61.4%). Majority of cases (87.1%) of rabies had history of dog bite. Though 50.5% patients received wound treatment, in only 5.9% cases it was adequate. Out of 23.8% patients having history of post-exposure vaccination, 75% of them received Nerve Tissue Vaccine (NTV) and 54% took vaccine in adequate doses and duration. Although 89.1% patient had history of WHO category III bite, none of them received Rabies Immunoglobulin (RIG). Furious rabies was seen in 97% cases. Majority (69.3%) patient develop rabies within 60 days of exposure and most of the rabies cases (68.4%) died within 72 hours. To prevent further human death from rabies and economic loss, educating people about preventive measures, Tissue Culture Vaccine (TCV) and RIG should be immediately introduced at primary health care level of Bangladesh.*

**Key words :** Rabies; Nerve tissue vaccine; Rabies immunoglobulin; Tissue culture vaccine.

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### Introduction

Rabies, a zoonotic disease caused by a neurotropic RNA virus, is endemic in most part of the world. In the year 2005 there were reports estimating that nearly 60000 human fatalities occur each year mostly in Africa and Asia [1]. According to World Health Organisation (WHO) every year 1550 people die of rabies in Bangladesh, makes this country ranking third in the world after India and China. A survey by disease control unit of Directorate General of Health Service (DGHS) shows that number of rabies death is more than 2000 per year and recent vaccine consumption shows post exposure vaccination is received by more than 100000 persons per year and a good number of victims of animal bite remain untreated [2].

Rabies is transmitted to human through exposure to saliva from infected animals (From bites, scratches, or licks on broken skin and mucous membranes). Dogs are mainly responsible for the transmission of rabies to human in this country [3]. Cat and jackal bite cases are reported in less than 10% of the total cases who seek care at health care facilities [4].

Diagnosis of rabies is challenging because of long incubation period (20-60 days on average, with rare reports of 5 to 6 days and up to 7 years) and lack of specificity of early prodromal symptoms and neurologic symptoms and also in absence of point-of-care pathological test [5].

In many patients, first symptom of rabies is itching, pain or paresthesia at the site of a healed bite wound. Prodromal symptoms then develop, including fever, myalgia, headache, irritability, depression, and upper airway or gastro-intestinal symptoms. A radiculopathy or other symptoms involving the bitten limb are often complaints of before encephalopathic syndromes develop. In the critical stage, most commonly signs of hyperactivity 'furious rabies' or less commonly paralysis-'dumb rabies' dominate. In both furious and dumb rabies, some paralysis eventually progress to complete paralysis followed by coma and death [6].

Diagnosis of rabies is made on clinical grounds and laboratory facilities are very limited in our country, virtually nonexistent.

About 150 cases of human rabies attend the Infectious Disease Hospital (IDH) Dhaka every year. This figure has not been changed too much over the last 5-10 years, indicating the urgent need to review the approach in preventing rabies in Bangladesh. Seven hundred and ninety four (794) rabies cases attended the IDH, Dhaka alone in a five year period [7]. There is no systematic record of clinical aspects of the cases of rabies in Bangladesh.

So this study has been carried out in Infectious Disease Hospital, Dhaka, Bangladesh to find out the clinical presentation of rabies, age group at risk, state of vaccination and wound care after exposure, interval between animal exposure and development of disease, interval between development of symptoms and death.

#### **Materials & methods**

This prospective case series carried out in Infectious Disease Hospital (IDH) Dhaka from June 2009 to August 2010. All the clinically diagnosed cases of rabies (Based on appropriate history of rabies prone animal exposure with clinical symptoms and signs of rabies) referred to IDH were included in the study. The data was collected from the patient attendant by trained emergency medical officer of Infectious Disease Hospital (IDH) by using a structured questionnaire. Necessary details were not available in some cases because of the ignorance of the relatives about the facts and were not included in the study. Patient having previous neurological or psychiatric diseases that may be confused with rabies, also excluded from study. Before starting the study, all emergency medical officers of IDH was briefed regarding data sheet. An explanatory note sheet was attached with data sheet to clarify different terms. Whenever possible information was verified by personal interview. Written and verbal consent was taken for using data and pictures of patient.

This structured questionnaire included data on age, sex, rural /urban, details of exposure to animal (Animal type, nature of exposure, site and number of bite, WHO category of wound), vaccination details (Pre-exposure, post-exposure prophylaxis) about wound treatment, interval between animal bite and development of rabies, symptoms of rabies, interval between appearance of symptoms and time of death. Patients wellbeing was collected from attendance of patient over mobile phone- that given during registration. The data were analyzed and compiled accordingly.

#### **Results**

Among one hundred four (104) rabies cases, attended in emergency department of Infectious Disease Hospital (IDH) Dhaka from June 2009 to August 2010, one hundred one (101) cases were finally included in study. Three cases having features of furious rabies, later on found alive without any supportive treatment were excluded from the study. Probably they were not rabies cases. Out of 101 cases, 70.3% were male, 29.7% were female. The age range of the patients was as low as one year and as high as 70 years. The median age was 10 years, and the mean age was 19.5 years. Most of the cases (61.4%) affect age group 1 to 15 years. Most of the rabies cases (85.2%) had come from the rural area.

In this study majority of the cases of rabies had history of dog bite/scratches (87.1%). Other animal involved were cat (7.9%), fox (3%), mongoose (1%), cow (1%). Pet animals transmitted the disease to human in 19.8 % and wild/stray animals were responsible in 80.2 %.

Considering nature of exposure, 95 patients (94.06%) had history of bite, 6 patients had history of scratch (including one patient having history of both bite and scratch). Most of the cases (56.44%, n=57) were bitten in the lower limbs while upper limbs were involved in 30.69%(n=31) cases. Twelve patients had history of bite at multiple parts of body. Fifty four (53.47%) cases had multiple wounds and forty seven cases had single wound. Of 101 cases 90 patients (89.1%) had WHO category III bite and 11 patients (10.9%) had WHO category II exposure.

Regarding vaccination history, no patient had history of taking pre exposure prophylaxis and post exposure Rabies Immunoglobulin (RIG) injection. Out of 101 patients, only 24 patients (23.8%) had received post exposure anti-rabies vaccine. Among the patient with positive vaccination history, 75% (n=18) received nerve tissue vaccine and 25 % (n=6) received cell culture vaccine. None of the cell culture vaccinated completed schedule. Thirteen patients who took vaccine in adequate dose and completed schedule are nerve tissue vaccinated.

**Table I :** Vaccination history of the patients (Post exposure prophylaxis) (n=101)

Vaccination history	Number (percentage)
Absent	77(76.2%)
Present	24 (23.8%)
Nerve tissue vaccine	18 (75%)
Cell culture vaccine	6 (25%)
Adequate dose	23 (95.8%)
Complete course	13 (54.2%)

(\* Post exposure vaccination: Dose adequate: vaccination by cell culture vaccine - 1 ml intramuscular, same dose for adult and children. Vaccination by nerve tissue vaccine ; Age <6 years - 2.5 ml, Age >6 years add 0.5ml for every 2 years increase of age, > 15years - 5ml once daily subcutaneously around umbilicus .Course complete means cell culture vaccine on day 0, 3, 7, 14, 28.If the patient has history of pre exposure prophylaxis-booster vaccine on day 0 and 3.Vaccination by nerve tissue vaccine above mentioned dose for 14 days).

Although 51 patients (50.50%) received wound treatment, only three patients had received it adequately. Out of 101 patients, 23.8% developed symptoms of rabies between 0 to 30 days of animal bite, while 45.5% of cases become symptomatic between 31 to 60 days. Minimum incubation period was 15 days and maximum was 730 days. All the patients (101,100%) died in this case series.

**Table II :** Interval between animal bite and development of symptoms (n=101)

Interval in days	Number (%)
<30	24 (23.8)
30 to 60	46 (45.5)
60 to 90	16 (15.8)
>90	15 (14.9)

**Table III :** Symptoms and Signs of rabies among subjects (n=101)

Symptoms/Signs	Frequency (%)
Itching at bite site	19 (18.8)
Headache	32 (31.7)
Restlessness	75 (74.2)
Hydrophobia	95 (94)
Aerophobia	97 (96)
Agitation	48 (47.5)
Unconsciousness	5 (4.9)
Dysphagia, hoarseness, quadriplegia	3 (2.9)

**Table IV :** Interval between symptoms onset and death (n=101)

Interval in hours	Number of cases (%)
<24	15 (14.9)
25 to 48	30 (29.7)
49 to 72	24 (23.8)
>72	32 (31.6)

### Discussion

Rabies is a fatal but preventable disease and a public health problem in Bangladesh [8]. Appropriate wound care and adequate post-exposure prophylaxis with a cell culture vaccine and rabies immunoglobulin following WHO guidelines can prevent most episodes of rabies [9,10].

In this study, like other studies mostly children are victims [11,12]. In this study, dogs were responsible for more than four-fifth of the case (87.1%) like Hossain et al (90.7% case). In our study, most (80.2%) cases were due to stray with wild animals and less (19.8%) due to domestic animals. Our finding suggests all potential pets capable to transmitting rabies should be adequately vaccinated.

Although 90 patients had WHO category III exposures, none received RIG. Therefore, optimum post-exposure prophylaxis was not given in these cases. Since, it takes at least 10 days to produce immunity following primary vaccination. RIG is an essential component of rabies post exposure prophylaxis [13].

None of the patients in this study had a history of rabies pre exposure prophylaxis. 76.2% of the patients had no history of vaccination. Of the 24 patients who had received a rabies vaccine, 18 received the NTV from Institute of Public Health and 6 received tissue culture vaccines. No patients received RIG, probably due to ignorance, high price and unavailability in most parts of Bangladesh. RIG is not prescribed very often even when it is available similar to a study from Pakistan [12]. Although half of cases received wound treatment, it was not adequate. Despite vaccination in adequate doses and duration, 13 people developed rabies (All received the NTV vaccine) probably due to poor efficacy of the vaccines, not having received RIG and poor wound care. In Pakistan, 67% of the bite victims received post exposure prophylaxis with a NTV without RIG and only 40% completed the full

course of vaccination [12]. Poor efficacy of the NTV suggests it should be eliminated and replaced with the Tissue Culture Vaccine (TCV). None of the victims who received the Tissue Culture Vaccine- completed the course. Our results show the TCV and RIG should be used and made available as recommended by the WHO. The high cost of the TCV and RIG hinder their use significantly. To achieve the target of preventing and control of rabies by the year 2020, the NTV will be phased out and the TCV will be phased in using 3 steps. Step 1 (2010-2011) TCV will be made available at IDH in Dhaka. Step 2 (2011-2012) TCV will be made available at Divisional Medical College Hospitals, City Corporations and IDH, Chittagong. Step 3 (2012-2013) TCV will be made available at the Upazilla Health Complex and in Pouroshava (DGHS, Bangladesh, 2010). Several measures may be taken to reduce the cost of PEP. Converting the facility at Institute of Public Health (IPH) to produce TCV might reduce the cost than imported vaccine. The introduction of intradermal TCV regimen and introduction of equine RIG might reduce the cost substantially [14,15].

In this study the minimum incubation period was 15 days and maximum period was 730 days. Maximum (n=70) patients developed rabies within 60 days of animal bite. In the Philippines, they found the maximum incubation period to be five years, although in 95% cases rabies developed within a year [16]. So it is better to start the vaccine as early as possible.

Main presenting features of rabies were hydrophobia, aerophobia, restlessness, agitation and headache. In this study most of the patients (69.3%) died within 72 hours of appearance of symptoms and 83.2% patients died within 24 hours of reporting to hospital. Thus furious rabies patient died within short time of appearance of symptoms as seen in other study.

People still do not know what to do after a rabies prone animal bite even at the cost of life of their family member, as seen in this study. Modern costly tissue culture vaccines though recently provided by Institute of Public Health (IPH) vaccines and rabies immunoglobulin should be available at primary health care level. Vaccination of pet animals should make mandatory.

### Conclusion

Rabies is an almost 100% fatal disease but 100% preventable if correct post exposure prophylaxis is carried out. Special emphasis on preventive measure and campaigning about it in print and electronic media, coordinated actions from different government and non-government organization is needed if we ever to reach the goal of prevention and control of rabies by the year 2020 in Bangladesh.

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### Disclosure

All the authors declared no competing interest.

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