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Original Research Article

A study of human rabies in adults admitted at infectious diseases Hospital of Tertiary Care Centre

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Abstract

Aims and Objectives: To study epidemiological characteristics and clinical profile with specific attention to non classical/atypical clinical presentation and deficiencies/lacunae in post exposure prophylactic management as per WHO guidelines in adult rabies patients.

Method: In this observational study, 96 cases of adult human rabies admitted at IDH of parent institute in 5 years duration (1/11/2008 to 31/10/2013) were studied. Data were collected and analyzed statistically.

Results: Majority (95.9 %) of victim's belonged to lower and lower middle socioeconomic class predominantly males (76.05 %) in age group of 12- 50 years (70.8 %) with WHO category III exposure (72.92 %). Principal biting animals was dog (95.84%). Majority (44.79%) cases had incubation period between 31-90 days post-exposure. Hydrophobia is the main pathognomonic feature of human rabies was present in 88.54 % cases. Majority (91.7 %) of cases had not received any rabies vaccination. 8.3 % victims received anti-rabies vaccine, 7.3 % received PCECV and 1% received PDEV. 1% had completed the course of PCECV (5 doses as relevant) and another 4.2% had received the 3 doses PCECV, 2.1% cases received 2 doses of PCECV. One case (1%) received 1 dose of PDEV.

Conclusion: Human rabies is a major health problem, equally affecting rural as well urban population. The epidemiological characteristics and clinical profile of the disease are not much different from other studies and have not changed much over the decades. Hence, there are need to educate the community and health workers about the importance of immediate and adequate post-exposure treatment, to start effective control program for dog and to make availability of TCV as well as RIG.

Keywords: Rabies, Anti rabies vaccines, Hydrophobia, Pathognomonic feature, Epidemiology.

1. Introduction

Rabies threatens millions of people in developing countries. Tens of thousands of victims die each year, despite it being a vaccine-preventable disease [1]. There are no universally accepted effective treatments for rabies once clinical symptoms are manifest. Human rabies primarily diagnosed on basis of clinical symptoms/signs and a corroborative history or evidence of animal bite, death of animal and incomplete or no vaccination following exposure. Facility of laboratory diagnosis and confirmation of rabies is available in only few institutions in India. Attempts to treat symptomatic patients infected with dog RABV variants with therapeutics and intensive care support are usually unsuccessful. A few patients who survived infection with bat RABV variants with good functional recovery had evidence of an early immune response, measured by neutralizing or non-neutralizing antibody to RABV in blood and CSF, with no RNA or virus detected in samples of biological fluids or hair follicles [2]. Therefore, a good outcome might depend on the promptness of the host response in the eradication of virus in both the CNS and periphery [2].

In order to achieve effective control of rabies, well designed surveys, data collecting system and surveillance are needed. Epidemiological studies of rabies required to

address several questions, for instance, what kinds of animal are the major carriers of the disease, how many people get rabies, how and why they get disease, which areas of the country have high incidence, how to prevent people from getting rabies, and how to control or eliminate this disease [3]. Clinical symptomatology is complex and commonly causes confusion to physicians. Because of the clinical diversity during the acute neurological phase, rabies can be distinguished as classic (encephalitic or furious and paralytic or dumb forms) and non-classic forms. Encephalitic and paralytic rabies also differ in the morbidity period (interval between clinical onset and death). Therefore, all health-care providers should aware of clinical feature of disease and should diagnose and differentiate rabies from other diseases [4].

Hence the present research was undertaken, to study epidemiological characteristics and clinical profile with specific attention to non classical/atypical clinical presentation and deficiencies/lacunae in postexposure prophylactic management as per WHO in adult rabies patients admitted in 5 years of period at IDH of our parent institute.

2. Materials and Methods

During the period of 5 years (From November 2008 to October 2013), a total of 171 suspected and probable cases of rabies were admitted at Infectious Diseases Hospital of parent institute. Out of 171 patients, 42 adult patients went LAMA after admission before outcome and 33 patients were pediatric patients (<12 years), hence were excluded from study. Thus remaining 96 adult patients were admitted till outcome i.e. death and they were included in study. This was an observational study conducted on 96 cases of adult human rabies having age > 12 years. Clinical case records of adult rabies patients admitted from 1/11/2008 to 31/10/2011 were analyzed retrospectively and from 1/11/2011 to 31/10/1013 rabies cases enrolled consequently, observed up to outcome in study period of 2 years (1/11/2011 to 31/10/2013). Patients with age <12 years and who leave against medical advice (LAMA) before outcome were also excluded from the study. The approval of ethical committee of our institute was obtained.

Data regarding distribution of age, sex and place of residence and socioeconomic status and seasonality, animal species involved, site of bite, type of exposure, duration between exposure and appearance of signs /symptoms, correlation to duration of appearance of signs/symptoms and site of exposure, category of exposure, presenting signs/symptoms, anti rabies prophylaxis treatment received before admission, treatment received after admission, survival time after appearance of signs/symptoms were collected and results were analyzed.

2.1 Statistical Analysis

Statistical software STATA version 10.0 was used for statistical analysis. Continuous variable were presented as Mean± SD. Categorical variable were expressed in actual number and percentages. For non normalized data, Median and range were calculated. Continuous variable were compared by performing unpaired t-test and Mann-Whitney test was applied for non-normalized variable. Categorical variable were compared by chi-square test. $P<0.05$ was considered as statistical significance.

3. Observations and Results

A total of 96 cases were enrolled in the study, having age between 13-80 years with mean age of 39.59 ± 17.80 years. The majority of patients 70.8% (68) were below 50 years of age (>12-50). Out of 96 cases, 76.05% (73) were males and 23.95% (23) were females. The male to female ratio was 3.17:1. More cases were from urban area 52.08 % (50) than 47.90 % (46) rural area. Majority (95.9 %) of victim's belonged to lower and lower middle socioeconomic class and remaining 3.1% (3) and 1% (1) cases were from middle and upper middle class respectively. 17 to 24 cases per year were admitted in our parent institute and there was no significant increase in particular year of study. No particular seasonality could be identified.

Table 1 shows distribution of cases in relation to animal species involved and type exposure as per WHO guidelines. Dogs were associated with source of infection in majority (95.84% (92) of cases. Most of the cases were bitten on lower 56.27% (54) or upper 33.34% (32) extremities. Head, neck or face bite was present in 7.29% cases. There were multiple bites involving trunk and upper limb in 1% (1) case. In 2.1% (2) cases there was no history of exposure available.

Table 1: Animal species involved and type of exposure as per WHO guidelines

Animal species	No. of patients (%)	Type of exposure	No. of patients (%)
Dog	92 (95.9%)	Category I	0 (0%)
Cat	1 (1%)	Category II	24 (25%)
Monkey	1 (1%)	Category III	70 (72.92%)
Wild animal	0 (0%)	Not known	2 (2.08%)
Not known	2 (2.1%)	-	-

The median duration of appearance of sign/symptoms after exposures was 75 days and mean duration was 131.73 ± 230 days, ranging from 13-1825 days. In 2.1% (2) cases exposure was not traceable. Overall

majority of cases (44.79%), duration between exposures and appearance of sign/symptoms was 31-90 days. Median duration of appearance of signs and symptoms after head, neck or face bite was 90 days (mean=116.42 ± 109.42 days, range: 15 -270), Upper extremities 60 days (mean=116.90 ± 206.16 days, range: 13 -1200 days) and lower extremities bite median duration was 84.5 days (mean=149.46 ± 260.36, range: 18 -1825 days). One case with multiple bites had duration 20 days. Statistically data was not significant (p-value=0.4790). The median duration of appearance of sign / symptoms with Category II was shorter [60 days (Mean=233.70 ±431.41days, range: 15 days -1825 days)] than Category III [75 days (Mean=100.54±78.17 days, range: 13 days -365 days)] which was statistically not significant. Table 2 shows the distribution of cases in relation to presenting complaints and combined symptoms of patients on admission. In present study most of patients presented with encephalitic phase of disease on admission.

Table 2: Presenting symptoms and combined symptoms of patients on admission

Presenting symptom	No. (%)	Presenting with combined symptoms	No. (%)
Hydrophobia	85 (88.5%)	Hydrophobia and excessive motor activity	47 (49%)
Excessive motor activity	56 (58.3%)	Hydrophobia and aerophobia	34 (35.4%)
Aerophobia	34 (35.4%)	Hydrophobia and fever	34 (35.4%)
Excessive salivation	31 (32.3%)	Hydrophobia and local pain	16 (16.7%)
Pain at bite site/limb	23 (23.6%)	Hydrophobia, aerophobia and photophobia	4 (4.1%)
Fever	23 (23.6%)	Hydrophobia and weakness	2 (2.1%)
Photophobia	5 (5.2%)	-	-
Weakness of limbs	2 (2.1%)	-	-
Other *	5 (5.2%)	-	-

(*=chest pain -2, loose motion -1, pain in abdomen-1, seizure-1)

Table 3 shows the distribution of sign and symptoms in studied patient after admission. Out of 96 cases were studied, clinical features of 97.9 % (94) were compatible with furious rabies and only 2.1% (2) were paralytic rabies.

Table 3: Distribution of clinical features in relation to form and stage of rabies cases

Clinical stage of Rabies	Clinical feature	No. of cases with feature (%)	
		Furious rabies	Paralytic rabies
Prodromal feature	Fever	35(37.2)	2(100)
	Parasthesia	0	0
	Local Pain	23(24.5)	0
	Vomiting	0	0
	Myalgia	27(28.1)	0
	Pruritus	0	0
	Excoriation	0	0
Encephalitic feature	Excessive motor activity	56(59.6)	0
	Hydrophobia	93(98.4)	2(100)
	Aerophobia	73(77.65)	1(50)
	Photophobia	47(50)	0
	Inspiratory spasm	16(17)	1(50)
	Seizure	1(1.1)	0
	Hypersalivation	31(33)	0
	Excessive lacrimination	0	0
	Tachycardia	63(67)	1(50)
	Piloerection	11(11.7)	0
	Perspiration	0	0
	Priapism	0	0
	Anisocoria	0	0
	Pupillary dilation	40(42.6)	1(50)
	Cerebellar signs	7(7.4)	0
	DTR exaggerated	28(29.8)	0
	DTR absent	0	2(100)
	Planter reflex Extensor	27(28.7)	0
	Planter reflex absent	6(6.4)	2(100)
	Crackles	23(24.5)	2(100)
Paralytic feature	Paralysis	0	2(100)
	Bladder dysfunction	0	1(50)
	Percussion myoedema	0	0
Other feature	Chest pain	2(2.2)	0
	Loose motion	1(1.1)	0
	Pain in abdomen	1(1.1)	0

After examination classic signs of rabies hydrophobia were present in 98.95 % (95) cases, aerophobia in 77.1% (74) and photophobia in 48.95% (47) cases while after examination of furious rabies cases classical signs of rabies; hydrophobia was present in 98.4% (93) cases, aerophobia in 77.65% (73) and photophobia in 50% (47) cases. All three features (Hydrophobia, aerophobia and photophobia) were present in 40.62% (39). Weakness of limbs was present in 2.15% (2) cases of paralytic rabies. In both cases of paralytic rabies weakness of limbs and hydrophobia was present and in one case aerophobia was present.

Table 4 shows distribution of cases in relation to post exposure local treatment received whereas table 5 shows distribution of cases in relation anti rabies treatment before admission in form of post exposure immunization and immunoglobulin. None of the patients received local treatment after bite as per advocated by WHO. Rabies developed in 1 case despite the fact that immunisation was performed at the appropriate time and with proper dose.

Table 4: Anti rabies prophylaxis before admission:-Local wound management

Type of local wound management	No. of cases (n=96)
Washing with Water	10 (10.4%)
Washing with soap and water	0 (0%)
Use of Antiseptic	37 (38.5%)
Suturing	00 (00%)
Not received any treatment	24 (25%)
Other*	25 (26.1%)

[*=Use of turmeric powder-3, lime-2, Magico-religious (faith healing, witchcraft, etc.) -18, Herbal therapy-2]

Table 5: Anti rabies treatment before admission: Post exposure immunization and Immunoglobulin

Type of vaccine	No. of cases	Number of doses (%)				
		1	2	3	4	5
Human Diploid cell Vaccine	0	0	0	0	0	0
Purified Chick embryo cell Vaccine	7 (7.3%)	1 (1)	1 (1)	4 (4.2)	0	1 (1)
Purified Duck embryo vaccine	1 (1%)	0	1 (1)	0	0	0
Total	8 (8.3%)	1 (1)	2 (2.1)	4 (4.2)	0	1(1)

All patients received sedation and supportive treatment in form of IV fluid and antibiotics. No patients received treatment after admission in form of antiviral therapy and intensive care. The mean survival time after appearance of signs and symptoms without intensive care in cases of paralytic rabies (mean = 7.5 ± 0.7 days, median = 7.5 days, Range: 7 - 8 days) was more than furious rabies (mean=4.52 ± 0.96 days, median = 4 days, Range: 3 - 8 days). Survival duration was statistically significant.

4. Discussion

In present study, the active age group of below 50 years had more outdoor activity more risk of exposure by rabid animals and development of rabies. The sex ratio in our study seems to be identical in all previous studies [5-8] and males affected twice or thrice as commonly female. This is probably because male have frequent outdoor activity as compared female and more frequent encounter with stray dogs leading to higher incidence of bite. 78.1% (75) cases were from Maharashtra and 21.9 % (21) from other states of India in which Madhya Pradesh contributed most 17.8 % (17). Our study setting was main tertiary referral center in government set up in this part of country, cases from neighboring districts and states referred here. More cases were from urban area 54.2 %(52) than 45.8 % (44) rural area. About 38.5% (37/96) of cases belonged to Nagpur city. The remaining 61.5% (59/96) cases were from the adjoining states and districts. However, if cases belonging to Nagpur city are excluded, more cases came from rural areas 74.6 % (44/59) than urban areas 25.4 % (15 /59). In rural areas, people work in the fields and are thus always exposed to the dogs and other rabid animals. In urban areas, people more exposed to the stray dogs, as high population of stray dog in urban areas of India. Most patients 95.9% (92) were from lower and lower-middle class whereas 3.1% (3) and 1% (1) cases from middle and upper middle Socio-economic class. This observation was identical with other studies [5,8] from developing countries.

Dogs were associated with source of infection in majority [95.84% (92)] of cases and there was no definite history of exposure to animals was available in 2.1% (2) cases. This observation was similar to that of other studies [6,7,9-13] carried out in developing countries. The most of the cases were bitten on lower 56.27% (54)) or upper 33.34% (32) extremities. Head, neck, face bite was present in 7.29% cases. There were multiple bites involving trunk and upper limb in 1% (1) case. In 2.1% (2) cases there was no history of exposure available. This observation resemble to other studies [5-8]. Lower extremities had been bitten more as these were exposed and accessible parts of body. Short statures get bitten close to head and neck. Hands and fingers had bitten, due to use of these parts of the body to

defend against the animal bite. Out of total 94 persons with known history bite, 72.92 % (70) had category III and 25% (24/96) had category II exposure. No history of exposure was known in 2.1 % (2/96) cases. In case of dog bite category of exposure usually depends on whether bite was provoked or unprovoked. In provoked bite category of exposure usually severe.

Out of 96 cases studied, clinical features of 97.9% (94) were compatible with furious rabies and only 2.1% (2) were paralytic rabies. The most frequent prodromal symptom was fever in 37.2% (35) cases of furious rabies and 100 % (2) cases of paralytic rabies followed by pain at the site of bite/limb in 28.7% (23) cases of furious rabies. Constitutional feature, myalgia was present in 28.1% (27) cases of furious rabies. The two most common signs of acute neurological phase were hydrophobia 98.4% (93) of furious rabies and 100% (2) cases of paralytic rabies, followed by aerophobia in 77.65% (73) of furious rabies and 50% (1) cases of paralytic rabies. Other sign of acute neurological phase like excessive motor activity was present in 59.6% (56) and photophobia in 50% (47) cases of furious rabies. Inspiratory spasms were present in 17% (16) of furious rabies and 50% (1) cases of paralytic rabies. 1.1 %(1) case of furious rabies seizure was presentation. Signs of autonomic nervous system dysfunction were, tachycardia in 67% (63) of furious rabies and 50% (1) cases of paralytic rabies, pupillary dilation in 42.6% (40) cases of furious and 50%(1) cases of paralytic rabies, hypersalivation 33% (31) and piloerection 11.7% (11) cases of furious rabies. Although many patients were not cooperative for CNS examination, in those examination was possible, after examination DTR were exaggerated in 29.8 % (28) cases of furious rabies. In both (100%) cases of paralytic rabies along with weakness of limbs DTR were absent. Extensor planter response was noted in 27 (28.7%) and was absent in 7.4% (7) cases of furious rabies. In both cases (100%) of paralytic rabies planer response was absent. Cerebellar signs in ere noted in 7.4 % (7) cases of furious form. No cases were noted with obvious cranial nerve involvement in encephalitic stage of disease. Most patients were not cooperative for sensory examination. After respiratory system examination bilateral crackles were noted in 24.5% (23) cases of furious rabies and 100% (2) cases of paralytic rabies in preterminal stage of disease.

On admission, 2 of 96 patients showed features of paralytic rabies, both presented with paralysis 100% (2), bladder dysfunction was observed in 50%(1). Other features like chest pain in 2.2% (2), loose motion in 1.1 %(1) and pain in abdomen in 1.1% (1) cases of furious rabies were noted. A female patient was presented with chest pain and altered sensorium, considering possibility of acute coronary syndrome she was admitted in ICCU. Electrocardiogram was within normal limit, next day phobic spasms were noted and history of dog bite was also traced. In our study, one 6 month ANC patient was presented with weakness of lower limbs; patient was admitted to medicine ward with provisional diagnosis of cortical sinuses thrombosis. Next day in that patient Inspiratory spasm, phobic spasms were noted and history of dog bite was traced, patient expired 4th day of admission at IDH with intrauterine death of fetus. Another young male patient was referred to our parent institute for acute onset ascending paralysis which was turned out to be paralytic rabies.

In present study, we thought peripheral institute/ medical practitioners referred only cases having characteristic features of furious rabies and history of dog bite and hence cases of paralytic rabies were less reported. So we advice any patient presenting with acute encephalitis, encephalomyelitis or acute onset paresis progressing rapidly to coma must be considered secondary to rabies unless proved otherwise. Laboratory confirmation of such cases should be done and diagnosis facilities should make available at tertiary referral health care centers. Besides knowledge of health care provider regarding rabies should updated with time.

In our study, no patients received local treatment after bite as per advocated by WHO. Out of 96 cases, 38.5% (37) victims had used antiseptic in local management. Out of these 37 patients 26 patients consulted local medical practitioner and received Tetanus Toxoid remaining 11 patients cleaned wound at home. Out of 26 patients who consulted medical practitioner only 8 patients received first dose of ARV. 26.04% (25) resorted to indigenous treatment in which approach most commonly resorted to were magico-religious practices 15.6% (15). 25% (24) cases not received any form of local prophylactic treatment. Only 1 patient had received all doses of ARV and no patient received anti rabies immunoglobulin. Majority viz. 91.7% (88) had not received any rabies vaccination. 8.3% (8) victims who had taken anti-rabies vaccine, 4.2% (7) had received PCECV and 1% (1) received PDEV. However, number of doses of vaccine received as ascertained from some households revealed that about 1% (1) had completed the course of PDECV (5 doses as relevant) and another 4.2% (4) had received the 3 doses PCECV. Two cases (2.1%) received 2 doses of PCECV one case (1%) received 1 dose of PDEV. Rabies developed in 1 case despite the fact that immunisation was performed at the appropriate time and with proper dose. The mean survival time after appearance of signs and symptoms without intensive care in cases of paralytic rabies was more than furious rabies. Survival duration was statistically significant (p-value=0.0130).

5. Limitations of study

1. Some of the clinical and epidemiological details of retrospectively studied were not available from the case records of the hospital
2. No laboratory diagnosis was done to confirm diagnosis.
3. Patients <12 years were excluded from study.
4. No intensive care / critical care management was instituted to patients.

6. Conclusion

Human rabies continues to be an important public health problem, equally affecting rural as well urban population. The epidemiological characteristics and clinical profile of the disease are not much different from other studies and have not changed much over the decades. Hence, there are need to educate the community and health workers about the importance of immediate and adequate post-exposure treatment, to start effective control program for dog and to make availability of TCV as well as RIG.

As we came across three non classical presentations on admission, the health care providers' right from primary to tertiary care centers needs to be sensitized for regular CME and other educational strategies. Even though we did not observed single case of rabies secondary to organ transplantation, we strongly believe in fact that all organ donors died of GBS/GBS like clinical features must be screened for rabies even in absence of possible history of exposure to rabid animal before organ transplantation, as increasing number of case reports of rabies secondary to organ transplantation are being published national and international publications. As we could not confirm the diagnosis of rabies in any of the victims due to non availability of resources, it is emphasized that confirmatory laboratory diagnostic tools and exclusively dedicated intensive/critical care facilities should be made available at least at tertiary care centres and medical teaching institutes. Albeit difficult but possible attempt of elimination /control of rabies in dogs needs to be priorotised to achieve the goal of "rabies free India by 2020."

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