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ORIGINAL ARTICLE

Rabies Vaccination Status among Occupationally Exposed Humans in Nigeria

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SUMMARY

Rabies virus, a bullet-shaped enveloped negative sense single stranded RNA virus, often carries death sentence once clinical manifestations commenced in humans and animals. Pre- and post-exposure vaccinations against the virus have long been in existence to protect humans, especially occupationally exposed such as workers in rabies laboratories, veterinary hospitals and clinics, wildlife rehabilitation centers and animal shelters. The need to receive this vaccination especially rabies pre-exposure vaccination becomes more important in endemic countries in accordance with Advisory Committee on Immunization Practise (ACIP). This study surveyed rabies vaccination status of occupationally exposed humans in Nigeria. The reasons adduced for unvaccination were also reported. Structured questionnaire were administered to veterinarians during the annual conference of Nigeria Veterinary Medical Association (NVMA) and the Continuous Education programme of Veterinary Council of Nigeria (VCN) in 2016 while others were administered at some wildlife facilities and animal shelters in Nigeria. Data were entered into SPSS version 23 for statistical analysis. Vaccinated and unvaccinated individuals were compared using univariate and logistic regression analyses to identify factors associated with vaccination status at $\alpha_{0.05}$ level of significance. Out of 250 questionnaires administered to veterinarians, wildlife managers and dog breeders (Group A) and 120 questionnaires administered to workers in veterinary practice, animal shelter & zoo garden/wildlife parks (Group B), only 155 and 83 questionnaires respectively were eligible and complete for analysis. The result obtained showed that 61.3% (95/155) and 85.5% (71/ 83%) of Group A and Group B respectively had not received pre-exposure rabies vaccination. Results of univariate analyses showed that health insurance were significantly associated with vaccination status in Group A and B while age was significantly associated with vaccination status for Group A only. This study showed that large number of occupational exposed humans did not receive rabies pre-exposure vaccination despite their frequent exposure to rabies sources (both domesticated and wild animals). Various impeding factors such as unavailability of rabies vaccines in the hospital, cost of vaccination, inadequate knowledge about rabies and its vaccination among other factors were presented and these should be taken seriously by both government and non-governmental organizations to ensure safety of this group of people.

Key words: Rabies, Vaccination, Nigeria, Occupationally exposed humans.

INTRODUCTION

Rabies is an ancient viral disease known to claim the lives of nearly 60,000 people annually worldwide (OIE, 2017). Its neuronal infection leading to nervous dysfunction and eventual death has been reported. It is a notifiable zoonotic disease and infected animals might not even show obvious and intense clinical sign of infection (in bat and dumb form in dogs) compared to the furious form described in dogs (MacLachlan and Dubovi, 2011). Rabies virus is a bullet-shaped virion belonging to the family rhabdoviridae, genus lyssavirus within the order mononegavirale (MacLachlan and Dubovi, 2011). It possesses an enveloped negative sense single stranded ribonucleic acid genome encoding five structural proteins (Fishbein and Robinson, 1993).

The virus is worldwide in distribution except in some countries where it has been declared rabies free or remained unreported (MacLachlan and Dubovi, 2011). Mammals including jackal, fox, wolf, skunk, raccon, bat, and dog can act as reservoir hosts of rabies virus (MacLachlan and Dubovi, 2011) and then transmit it to other animals. The most common route of transmission is by bite of a rabid animal, though other routes such as organtransplant and aerosol, are possible means (Takayama, 2005).

It has been reported that mortality rate of 38-57% is possible and even more in an untreated bite cases of rabid dog (Hemachudha *et al.*, 2002; Warrell and Warrell, 2004) though this depends on the virus load in the saliva in conjunction with location and severity of wound. Generally, case fatality rate of up to 100% has been reported in humans and animals already exhibiting rabies symptoms (Takayama, 2008; Willoughby *et al.*, 2005). In order to avert this great danger before and after infection, various rabies vaccines have been developed including Human Diploid cell vaccine (HDCV) and Purified Chick Embryo Cell Vaccine (PCEC), but these are not without side effects (CDC, 2011). Commercial Human rabies immune Globin (HRIG) has also been in existence for prophylactic treatment and recommended as part of post exposure rabies vaccination (CDC, 2011).

Although, the clinical feature of rabies varies, furious and dumb forms have been reported (WHO, 2016). Despite these forms, a definite diagnosis requires laboratory testing including electron microscopy (identification of Negri bodies in the neurons), direct immunofluorescene or immunohistochemical staining (demonstrate rabies viral antigen using brain tissue) or reverse transcriptase- Polymerase chain reaction (identify the rabies RNA). The gold standard serological test for rabies is Rapid Fluorescent Focus Inhibition Test (RFFIT) as recommended by World health Organization (WHO) and Advisory Committee on Immunization Practise (ACIP). Other serological tests such as Enzyme Linked Immunosorbent Assay (ELISA) are more appropriate in research rather than their use in clinical decision (CDC, 2016).

Individuals at risk of rabies virus infection are classified based on the likely exposure to the common sources of rabies virus and these people include rabies researchers, veterinarians, wildlife workers, dog breeders, hunters, animal handlers and veterinary students. These categories of people might even increase with increasing rabies case fatality rate in space and time (endemicity). Based on this, as preventive measure against rabies virus, rabies pre-exposure vaccination has been recommended to be offered to these categories of individuals by Advisory Committee on Immunization Practises (ACIP) published by Center for Disease Control and Prevention (CDC, 1999). The pre-exposure rabies vaccine regiment is a 3

to 4 dose series at weekly intervals (CDC, 1999). In addition, CDC recommends post vaccination rabies antibody titer check after 2 years for people with frequent exposure (frequent risk categories including veterinarians and staff, animal control and wildlife workers and caver) and 6 months interval for rabies research laboratory workers (Continuous risk categories) (CDC, 1999). Thus, rabies booster vaccine can only be administered when the rabies virus complete neutralizing antibody is less than 1:5 serum dilution using RFFIT (CDC, 2016).

Rabies pre-exposure vaccination series has been argued to simplify and reduce the cost of post-exposure vaccination in previously vaccinated humans. It also protects against unrecognized exposure to rabies virus.

Despite the availability of all necessary tools needed to eradicate or prevent rabies virus, death resulting from rabies lingers especially among children in developing countries (OIE, 2017). This study aimed to assess rabies pre-exposure vaccination among veterinarians and staff, wildlife workers and dog breeders who are occupationally exposed people in Nigeria. The reason(s) for lack of rabies pre-exposure vaccination among others were also reported. This research intends to guide the policy makers in order that the desire of preventing and eradicating rabies virus might be achieved in Nigeria.

MATERIALS AND METHODS

A cross-sectional survey was conducted using pre-tested structure questionnaire which were administered to veterinarians at the annual conference of Nigeria Veterinary Medical Association (NVMA) and Continuous Education programme of Veterinary council of Nigeria in 2016. Also, questionnaires were administered to animal handlers, wildlife workers and dog breeders in various parts of the country including Kwara, Oyo, Ogun, Osun, Plateau States and Federal capital territory, Abuja. An informed consent of only occupationally exposed humans who directly handled animals (domestic dogs and cats, and wildlife) was sort and thereby included in the study. Each respondent was given a copy of the questionnaire and was left to complete it.

Statistical Analysis

Data were entered into a Statistical package for Social Sciences (version 23, 2015) for descriptive data analyses. The analysis excluded anyone who was in the following categories: veterinarians who were no more in practice, non veterinarians who do not handle dog, cat and wild animals directly, anyone who did not fill the questionnaire completely by leaving out vital question(s).

Odds ratios (OR) and exact 95% confidence intervals (CI) were calculated for gender, age, facility type, position, employment duration and health insurance. Multiple logistic regressions were performed to further quantify associations between potential predictor variables and rabies vaccination status. Outcome (vaccination status) was coded as a dichotomous variable, with vaccinated persons considered to be positive for the outcome ($y = 0$) and unvaccinated persons considered to be negative for the outcome ($y = 1$). Dummy variables were generated for categorical variables with > 2 levels. Values of $P < 0.05$ were considered to be significant.

RESULTS

Veterinarian, wildlife manager and dog breeder respondents group

A total of 250 questionnaire were administered during the survey but only 190 questionnaire were returned among which 35 respondents were either not eligible based on ACIP criteria (office administrators and retired veterinarians) or didn't fill the questionnaire completely; thus leaving 155 persons for the analysis. One hundred and fifteen (74.2%) of the respondents were male (Table I). The

respondents in this group represented 135 Veterinary practices, 8 animal shelters and 12 Zoo garden/wildlife park. Ninety five (61.3%) of 155 respondents in this group had not received rabies pre-exposure vaccination series. Among the 60 (38.7%) vaccinated respondents, the interval from the day of last vaccination to the time of the survey ranged from 1 month to 34 years (median= 2years). Eighteen (11.6%) had received the pre-exposure series > 2 years previously, of which 5 (3.2%) were booster doses without having their rabies titer checked.

Employment duration of the respondent in this group ranged from 1 month to 52 years (median= 5years). Only 29 (18.7%) respondents had health insurance within which 12 (7.7%) were not sure whether it covers rabies vaccination, and 7 (4.5%) were unsure if having their rabies titer checked was covered. Among the unvaccinated respondents, 1 or more of the following were indicated as reason for not being vaccinated: high cost (8), unavailable in the

TABLE I: Distribution and analysis of rabies vaccination among Veterinarian, Wildlife manager, Dog breeder respondents in Nigeria

Factor	Freq. (%)	Vaccinated (n=60)	Unvaccinated (n= 95)	OR (95% CI)
Gender				
Male	115 (74.2)	46 (40.0)	69 (60.0)	1.22(0.51─2.91)
Female	40 (25.8)	14 (35.0)	26 (65.0)	1
Age (years)				
20-25	7 (4.5)	0 (0.0)	7 (100.0)	1
[a]26-30	28 (18.1)	11 (39.3)	17 (60.7)	0.01 (0 ─ 0.03)
[a]31-35	46 (29.7)	18 (39.1)	28 (60.9)	0.01 (0 ─ 0.03)
[a]36-40	28 (18.1)	12 (42.9)	16 (57.1)	0.01 (0 ─ 0.04)
[a]41-50	30 (19.4)	13 (43.3)	17 (56.7)	0.01 (0 ─ 0.03)
[a]>50	16 (10.3)	6 (37.5)	10 (62.5)	0.01 (0 ─ 0.02)
	135 (87.1)			1
Facility Type	8 (5.2)			6.43
Veterinary practice	12 (7.7)	54 (40.0)	81 (60)	(0.53─78.55)
Animal shelter		1 (12.5)	7 (87.5)	1.52
Zoo garden/Wildlife park		5 (41.7)	7 (58.3)	(0.23─10.04)
Position				
Practice owner/Facility manager	27 (17.4)	8 (29.6)	19 (70.4)	1
Associate veterinarian	110 (71.0)	43 (39.1)	67 (60.9)	1.24 (0.32─4.76)
Self employed veterinarian	18 (11.6)	9 (50.0)	9 (50.0)	0.6 (0.11─3.27)
Employment/working duration				
(Year)	80 (51.6)			1
≤5	39 (25.2)	30 (37.5)	50 (62.5)	1 (0.41─2.44)
6 – 10	14 (9.0)	16 (41)	23 (59)	0.73 (0.16─3.26)
11 – 15	4 (2.6)	6 (42.9)	8 (57.1)	0.27 (0.02─3.42)
16 – 20	18 (11.6)	3 (75.0)	1 (25.0)	3.91
≥21		5 (27.8)	13 (72.2)	(0.72─21.31)
Health insurance				
[b] Yes	29 (18.7)	16 (55.2)	13 (44.8) 76	0.11 (0.01─1.03)
No	119 (76.8)	43 (36.1)	(63.9)	0.24 (0.03─2.04)
Not sure	7 (4.5)	1 (14.3)	6 (85.7)	1

Key: OR- Odd ratio CI- Confident interval Freq.- Frequency [a] P< 0.01 and [b] P < 0.05

TABLE II: Distribution and analysis of rabies vaccination among workers in Veterinary practice, Animal shelter & Zoo garden/Wildlife park in Nigeria

Factor	Freq. (%)	Vaccinated (n=12)	Unvaccinated (n= 71)	OR (95%CI)
Gender				
Male	63 (75.9)	12 (19.0)	51 (81.0)	1
Female	20 (24.1)	0 (0.0)	20 (100.0)	(-∞ - ∞+)
Age (years)				
20-25	13 (15.7)	2 (15.4)	11 (84.6)	2.67e-16 (0 - ∞)
26-30	14 (16.9)	3 (21.4)	11 (78.6)	5.46e-09 (0 - ∞)
31-35	11 (13.3)	2 (18.2)	9 (81.8)	1.53e-08 (0 - ∞)
36-40	25 (30.1)	3 (12.0)	22 (88.0)	1.36e-08 (0 - ∞)
41-50	17 (20.5)	2 (11.8)	15 (88.2)	1.29e-08 (0 - ∞)
>50	3 (3.6)	0 (0.0)	3 (100.0)	1
Facility Type				
Veterinary practice	11 (13.3)	0 (0.0)	11 (100)	1
Animal shelter	13 (15.7)	1 (7.7)	12 (92.3)	3.28e-08 (0 - ∞)
Zoo garden/Wildlife park	59 (71.1)	11 (18.6)	48 (81.4)	2.11e-07 (0 - ∞)
Type of employment				
Full time	62 (74.7)	10 (16.1)	52 (83.9)	1
Part time	21 (25.3)	2 (9.5)	19 (90.5)	0.785(0.033 - 18.643)
Employment duration				
1 -11months	18 (21.7)	1 (5.6)	17 (94.4)	1.87e-08 (0 - ∞)
1 - 2 years	7 (8.4)	0 (0.0)	7 (100.0)	1
≥3 years	58 (69.9)	11 (19.0)	47 (81.0)	1.33e-15 (0 - ∞)
Health insurance				
Yes	25 (30.1)	10 (40)	15 (60)	1
[a]No	58 (69.9)	2 (3.4)	56 (96.6)	32.76 (2.98- 359.57)

Key: OR- Odd ratio CI- Confident interval Freq.- Frequency [a] $P < 0.05$

hospital (49), low perceived risk (29), concern about possible adverse effect (12) and aware but its importance is unknown (1).

All variables were then entered into a logistic regression model and data were analyzed to evaluate the association between vaccination status and socio-economic characteristics of these respondent group. Results of univariate analyses of data from these respondents indicated that only age and insurance were significantly associated with rabies vaccination status **(**Table I). The respondents who were ≥ 26 years old were less likely (OR, 0.01) than those who were ≤25 years old to have received rabies pre-exposure vaccination.

Veterinary practice, animal shelter & zoo garden/wildlife park workers respondents group

A total of 120 questionnaires were administered directly to the workers. However, 14 questionnaires were not returned while 23 out of the remaining 106 respondents were not included in the analysis because of non-eligibility and incomplete information provided. The analysis was left with 83 responses. Sixty three (75.9%) of the respondents were male (Table II). Age range of 36-40 years and >50 years had the highest and lowest number of workers 25 (30.1%) and 3 (3.6%) respectively. The respondents represented 59 (71.1%), 13 (15.7%) and 11 (13.3%) of Zoo garden/wildlife park, animal shelters

and Veterinary practices respectively. Fifty eight (69.9%) and 7 (8.4%) of the respondents had worked within these facilities for ≥3 years and 1-3 years respectively representing the highest and lowest value. Also, 58 (69.9%) of the respondents had no health insurance. Among those who had health insurance (25 respondents), 23 respondents indicated the insurance didn't cover rabies vaccination while the remaining 2 respondents indicated theirs covered rabies vaccination but not rabies titer checking.

Seventy one (85.5%) of the workers respondents had not received rabies pre-exposure vaccination series. Among the 12 (14.5%) vaccinated respondents, none but one indicated the date of last rabies pre-exposure vaccination. None of them indicated any booster dose of rabies vaccination. Among Fifty eight (69.9%) of the respondents who had worked within these rabies risk facilities for ≥3 years, 47 (81.0%) of them never received rabies pre-exposure vaccination. Among respondents without health insurance (n= 58; 69.9%), 56 (96.6%) indicated they had never received rabies pre-exposure vaccination.

Among the unvaccinated workers respondents, 1 or more of the following were indicated as reason for not being vaccinated: high cost (13), unavailable in the hospital (2), low perceived risk (10), concern about possible adverse effect (4), not aware (6) and aware but not educated about its vaccination (36).

Data were analyzed to evaluate the association between vaccination status and workers socio-economic features. Out of the variables that entered logistic regression model, only workers being insured were found to have a significant relationship with vaccination status (Table II). The results revealed that uninsured workers were more likely not to have received pre-exposure rabies vaccination, compared with those who were insured.

DISCUSSION

This data showed that 61.3% (95/155) and 85.5% (71/ 83%) of veterinarian, wildlife manager and dog breeder respondents group and veterinary practice, animal shelter and zoo garden/wildlife park workers respondents group respectively had not received pre-exposure rabies vaccination despite rabies endemicity in Nigeria and their frequent exposure to rabies sources (both domesticated and wild animals). The poor responses to rabies pre-exposure vaccination among veterinarians can be compared with the same among clinical veterinary medical students in Nigeria which stood at 17.4% (Daodu and Oluwayelu, 2016). In addition, Olugasa et al (2010) reported that 58.6% of occupationally exposed humans in a Nigerian University were not immuned and thereby leaving them at high risk of rabies infection.

In Nigeria, there is no regulatory requirement for dog breeders, wildlife workers and animal handlers to receive rabies pre-exposure vaccination or be educated about rabies risk at the work place. Unavailable of rabies vaccine in the hospital (n= 49; 31.6%) was the most frequent reason adduced by veterinarian, wildlife manager and dog breeder respondents group. Other reasons include "low perceived risk" (n= 29; 18.7%), "concern about possible adverse effect" (n= 12; 7.7%), "high cost" (n= 8; 5.2%), and "aware but its importance is unknown" (n= 1; 0.6%). Among veterinary practice, animal shelter and zoo garden/wildlife park workers respondents group, the reasons cited include "aware but do not know how to go about its vaccination" (n= 36; 43.4%), "high cost" (n= 13; 15.7%), "low perceived risk" (n= 10; 12.0%), "not aware" (n= 6; 7.2%), "concern about possible adverse effect" (n= 4; 4.8%) and "unavailable in the hospital" (n= 2; 2.4%). The causes for limited rabies vaccine supply in Nigerian hospitals might be due to cost of importation, frequency of rabies vaccination request and readiness to

pay for the service, sustainability of cold chain for rabies vaccine and government policies about rabies vaccination among occupationally exposed individuals. Generally, the cost of rabies vaccination is very high in Nigeria (Daodu and Oluwayelu, 2016). A shot of rabies vaccination can be up to 6,810 naira (at exchange rate of $1 = 300 naira) while 3-rabies shots (minimum as recommended by CDC) would likely cost 20,430 naira. Government should encourage people at risk to receive rabies pre-exposure vaccination as CDC advised by making it as one of the critical requirements for any facility where humans can be at risk of rabies infection. They should subsidize the cost of importation of human rabies vaccine, ensure its availability in the hospitals and its inclusion in National Health Insurance Scheme (NHIS) at a bearable price. In addition, workers in veterinary hospitals, animal shelters and wildlife parks should be properly educated about the risk of rabies and "where, how and when" to receive rabies vaccine. The result also showed that among 60 (38.7%) vaccinated respondents (veterinarian, wildlife manager and dog breeder respondents group), only 5 (3.2%) respondents received booster rabies doses and none of these checked their rabies antibody titer. The facility for Rapid Fluorescent Focus Inhibition Test use in determining rabies antibody titer to making decision whether or not a rabies booster is needed should be made readily available and at affordable price.

The veterinarian, wildlife manager and dog breeder respondents group, there were statistical differences in age and health insurance as related to rabies pre-exposure vaccination ($P< 0.05$) while among workers in veterinary practice, animal shelter and zoo garden/wildlife park, health insurance was statistically significant ($P< 0.05$). This study was limited in that rabies antibody titer was not quantified to ascertain the protection status of vaccinated individuals in this study.

CONCLUSION

This study showed that most of the occupationally exposed humans in Nigeria were not vaccinated with pre-exposure rabies vaccine; thereby increasing their chances of rabies infection. We recommend that concerned government ministries and professional bodies should look more closely into rabies pre-exposure vaccination among people working under facilities which put them at high rabies risk. A sound and workable zoonotic diseases control policy should be formulated. The regulating body can also make rabies pre-exposure vaccination as a requirement for workers in these rabies risk facilities.

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