

HUMAN RABIES IN SOUTH AFRICA, 2012-2013

Veerle Dermaux-Msimang, Jacqueline Weyer, Janusz Paweska

Centre for Emerging and Zoonotic Diseases, NICD

Introduction

Rabies is a zoonosis causing fatal encephalitis. The disease is caused by the rabies virus and other so-called rabies-like viruses belonging to the genus *Lyssavirus*. From a public health perspective, the rabies virus is the most important and causes an estimated 55 000 human cases in developing countries annually.

Rabies cases occur widely in Africa, including South Africa, mostly as a result of inadequate control of rabies in domestic dogs. In South Africa, the rabies virus is maintained in complex epizootic cycles involving domestic dogs, black-backed jackals, bat-eared foxes and several species of herpestids (i.e. mongoose and suricates).¹ In South Africa, 85% of laboratory confirmed human cases have been associated with domestic dogs while the remainder are likely the result of exposure to game animals.² Historically, the majority of human rabies cases in South Africa have been reported from the KwaZulu-Natal and Eastern Cape provinces but, more recently, an increasing number of cases have been reported from Limpopo Province. In the past decade, rabies has been described from locations where it was previously controlled. This includes the Vhembe district of the Limpopo Province³ and southern and eastern-southern Mpumalanga.⁴ The first report of local transmission of rabies virus in Johannesburg, Gauteng Province, was reported in 2010.⁵

Laboratory confirmed human cases

The National Institute for Communicable Diseases (NICD) has been involved in the laboratory investigation of human rabies cases in South Africa since 1983. From this time to date, a total of 420 human rabies cases has been laboratory confirmed. Of these, 137 have been reported in the past ten years (2003-2013) with an average of 12.45 cases per year (range: 6-31 cases per year). Two thirds of these cases (n=104) were male with an average age of 17.6 (range 1-80). The majority of cases were of the younger age group with 46% aged below 9 years. Cases were reported from the KwaZulu-Natal (n=52), Limpopo (n=39), Eastern Cape (n =32), Mpumalanga (n=6), Free State (n=4), North West (n=2), Northern Cape (n=1) and Gauteng (n=1) provinces.

During 2012 and 2013 a total of 17 cases was recorded. These were reported from the Limpopo (n=6), KwaZulu-Natal (n=5), Free State (n=3), Mpumalanga (n=2) and Eastern Cape (n=1) provinces (figure 1, table 1). A history of dog exposure was described in fourteen of these cases (82.35%).

The NICD has the capacity for ante-mortem and post-mortem investigations of suspected human rabies cases. During 2012-2013, 14 of 17 confirmed cases were tested by the direct fluorescent antibody test on brain impression smears. This test remains the gold standard for laboratory diagnosis of rabies.

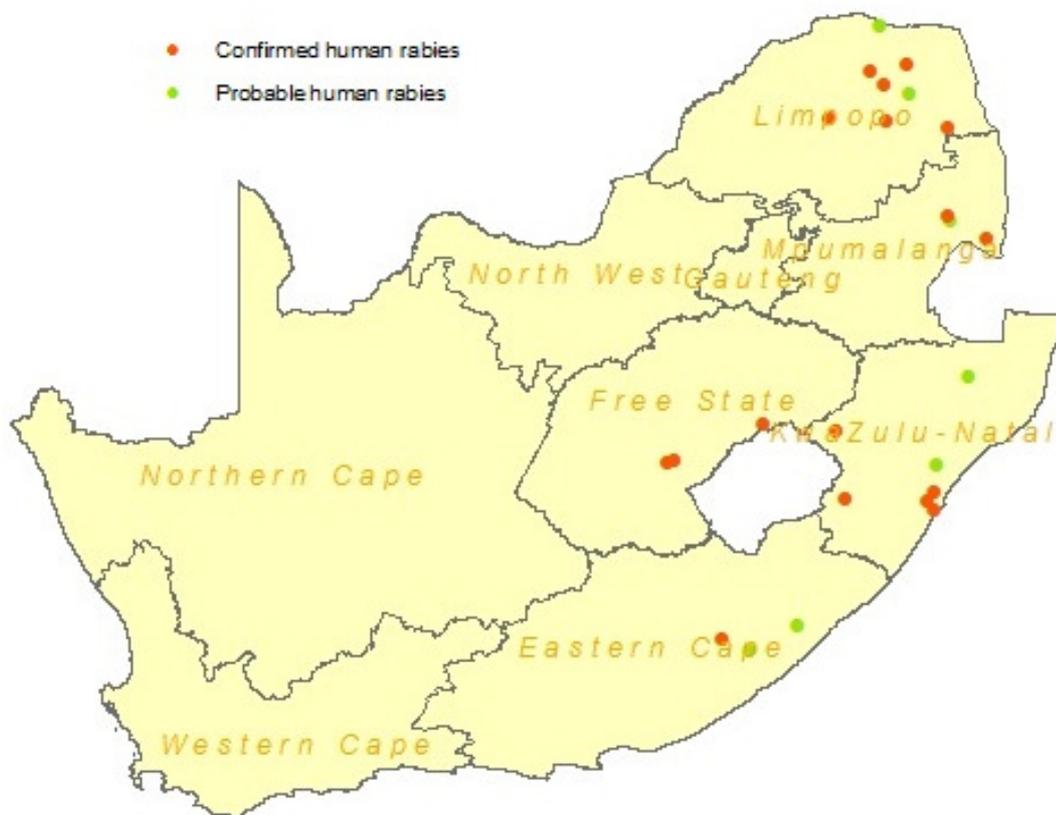
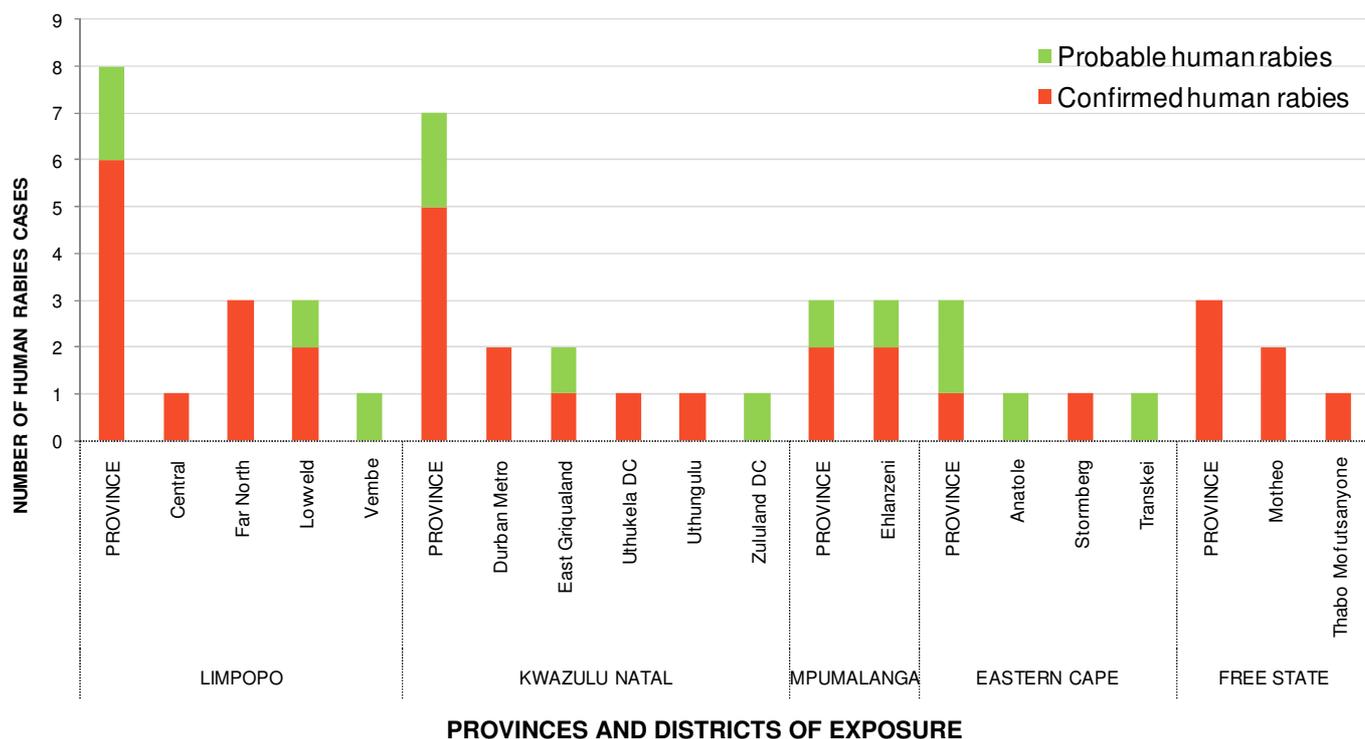


Figure 1: Distribution of laboratory confirmed and clinically diagnosed human rabies cases by province and district in South Africa, 2012-2013.

Table 1: Case details of laboratory confirmed human rabies in South Africa, 2012-2013.

Year	Age/ Sex*	Location residence/ exposure	Source of exposure	Category of exposure	Post exposure intervention	Symptoms
2012	2M	Chebeng, Limpopo	Dog	Below the eye category 3	4 doses rabies vaccine, no rabies immunoglobulin	Fever, confusion, loss of ability to walk
2012	17F	Thohoyandou, Limpopo	Unknown	Unknown	Unknown	Fever, confusion, developed left hemi-paresis
2012	29M	Underberg, KwaZulu-Natal	Dog	Unknown	None	Migratory pain up arm into head, hydrophobia, breathing difficulty, dysphasia, delirium, confusion, agitation, photophobia
2012	52F	Engonyameni, near Umlazi, Kwazulu-Natal	Dog	Bite on right arm category 3	None	Itchiness and pains on the site of the healed wound bite, hydrophobia, hypersalivation, confusion, weakness, vomiting, brain scan showed encephalitis
2012	7M	Bergville, Okhahlamba, Kwa- Zulu-Natal	Dog	Single bite on fore-arm, category 3	None	Malaise, loss of energy, confusion, vomiting, fever
2012	8M	Nkomazi, Mpumalanga	Dog	Unknown	None	Unknown
2012	10M	Mukulamu, kondeni, Nukula, Limpopo	Unknown	Unknown	None	Six days history of fever, confusion, inability to walk or sit
2012	21M	Tshelimnyama, Mariannhill, KwaZulu-Natal	Dog	Palm of left hand category 3	One dose rabies vaccine, no rabies immunoglobulin, wound treatment	Nausea, headache, pain to left shoulder and arms, palpitations, difficulty in swallowing and hydrophobia
2012	10M	Fouriesburg, Free State	Dog	Two bites on face/ nose and arm category 3	Referred for suturing , tetanus vaccination, no rabies post exposure prophylaxis	Difficulty in swallowing, could not swallow water
2012	7M	Ncoaha A/A, Ematheleni Village, Cofimvaba, Eastern Cape	Dog	Wound on left hip category 3	One dose of rabies vaccine, no immunoglobulin	Fever, headache, vomiting, muscle spasm, anorexia, priapism, localised weakness, confusion, agitation, autonomic instability, malaise, anxiety, dysphasia, delirium, aggressiveness, hypersalivation
2013	6M	Malukazi, southern border of Umlazi, KwaZulu-Natal	Dog	Wound right hand, buttock and left wrist, multiple bites category 3	4 doses rabies vaccine, no immunoglobulin	Fever, headache, muscle spasm, coughing, vomiting, malaise, nausea, dysphasia, anorexia, developed pain in the back of her left leg and in her arm, confusion, anxiety and impaired communication
2013	65M	Mvangatini, Kabokweni, Mpumalanga	Dog	Wound index finger, right hand single bite category 3	One dose of rabies vaccine, no immunoglobulin	Headache and pain in hand that sustained wound, aero-and hydrophobia, hypersalivation, confusion, instability and anxiety
2013	21M	Thaba-Nchu, Mangaung, Free State	Dog	Wound, category 3, undescribed	Wound treatment only, no rabies post exposure prophylaxis	Difficulty in swallowing own saliva and water, hydrophobia, increased temperature, confusion, agitation
2013	9F	Elim, Makhado, Limpopo	Unknown	Unknown	None	Neurological syndrome, hyperactivity, coma
2013	5M	Botshabelo, Free State	Dog	Superficial wounds/scratches category 2	Unknown	Confusion, hypersalivation
2013	38M	Mopani, Elim, Limpopo	Dog	Single bite on calf of leg, category 3	None	Fever, muscle spasm, insomnia, anxiety, seizures, hydrophobia, hypersalivation, clenching teeth, WBC normal
2013	38M	Tzaneen, Limpopo	Dog	Undescribed, category 3	None	Severe headache 3 days, painful joints, dizziness, confusion, restlessness, pyrexia, hydrophobia 2 days

*Age is given in years; M=male; F=female

Intervention failure in confirmed human rabies cases

Nearly half of the laboratory confirmed human rabies cases apparently did not seek any medical intervention after exposure to rabid animals (figure 2). This reflects the general lack of awareness of the public of the importance of seeking post-exposure prophylaxis upon contact with suspect animals, especially dogs. It must also be taken in consideration that the majority of confirmed rabies cases are from rural areas and that

access to medical care may be problematic. In two cases, the patients presented to health care facilities but were provided only with wound treatment reflecting the lack of awareness of the healthcare workers.

Another important contributing factor to failure in prevention of rabies virus infection was the non-provision of rabies immunoglobulin (RIG) in category 3 exposures. This is a known and well document reason for so-called rabies post exposure prophylaxis failures.⁶

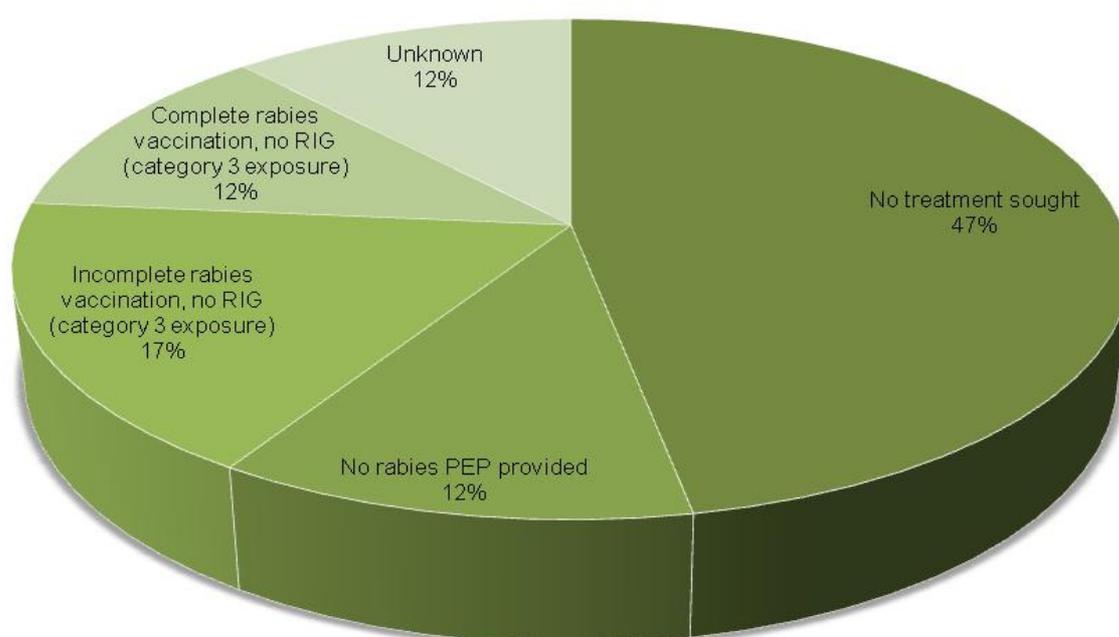


Figure 2: Interventions for rabies prevention in laboratory confirmed human rabies cases, South Africa, 2012-2013

Clinically diagnosed human cases

During 2012 and 2013, a total of seven cases of rabies with clinical diagnosis was recorded. These originated from the Limpopo (n=2), Eastern Cape (n=2), KwaZulu-Natal (n=2) and Mpumalanga (n=1) provinces (table 2). Five of these cases are classified as probable cases as defined by the World Health Organization.⁷ The case histories included animal exposure and the clinical progressions and outcomes were compatible with

rabies disease. These cases could not be verified by laboratory testing for various reasons: in two cases extensive ante-mortem investigation yielded only negative results and no specimens were available post-mortem for confirmation; all testing, including direct fluorescent antibody performed on post-mortem collected brain tissue, was negative for one case; no tissue samples were submitted for investigation for one of the cases from the Limpopo Province.

Various factors contribute to the failure of laboratory confirmation of cases. Although ante-mortem testing is useful, the direct fluorescent antibody test performed on brain biopsies remains the gold standard for rabies laboratory diagnosis. However, obtaining brain tissue post-mortem from patients that died of suspected rabies disease can be problematic due to cultural and religious beliefs and consent is often denied. Ante-mortem investigations should be based on comprehensive testing of repeat saliva specimens, nuchal biopsies,

cerebrospinal fluid and serum. The latter are used for the detection of rabies antibodies which may indicate seroconversion in unvaccinated individuals, whilst the other specimens are screened for the presence of viral RNA. The quality of the specimens and vaccination history of each patient are some of the factors that may influence test outcomes. Negative test results on ante-mortem collected specimens do not exclude a diagnosis of rabies.

Table 2: Case details of clinically diagnosed cases of human rabies, South Africa, 2012-2013.

Year	Age/ Sex*	Location residence/ exposure	Source of exposure	Category of exposure	Post exposure intervention	Symptoms	Out- come	Laboratory investigations for rabies	Classifi- cation ¹
2012	16M	Tafalofefe, Eastern Cape	Dog	A bite on left calf, category 3	3 doses rabies vaccine, no rabies immunoglobulin	Fever, headaches, inability to walk or talk, confusion, coma within a week	Death	saliva & CSF - by PCR, CSF + IgG/M IFA, ante-mortem skin biopsy, saliva - by PCR, no post-mortem	Probable
2012	4M	Ngonyami school, Umlazi, KwaZulu- Natal	Dog	Multiple bites left lower ankle, category 3	3 doses rabies vaccine, no rabies immunoglobulin	Confusion, talking by himself, loss of appetite, incontinence and suffering, seizure, neck stiffness, hyper salivation and unresponsiveness.	Alive	5 x saliva, nuchal biopsy – by IFA	Probable
2013	2M	Botshabelo, Limpopo	Dog	Unknown	1 dose rabies vaccine, no rabies immunoglobulin	Biting infusion line, refusal to eat, talking to himself, unable to walk, weakness, aggres- sion, diarrhoea, meningitis- like illness	Death	No specimens submitted	Probable
2013	7M	Ncwasa, Mqwanduli, Eastern Cape	Unknown	Unknown	Unknown	Refusal of food despite appe- tite, vomiting, weakness, mild wheezing in chest, act in strange manner, looked confused, restless, hypersali- vation, failed resuscitation, itching at vertical side of knee	Death	No specimens submitted	Suspected
2013	40F	Zululand, KwaZulu- Natal	Cat	Scratches, category 2	None	Headache, nausea, vomiting, hypersalivation, hydrophobia, confusion, restlessness	Death	Serum & CSF - by IG/M IFA, saliva, skin biopsy - by PCR & impression smears, brain - by FAT	Probable
2013	22M	Msogwaba, Mpuma- langa	Unknown	Unknown	unknown	Seizures, meningitis, constantly scratching healed wound on his left leg	Death	saliva & CSF - by PCR, blood & CSF + by IG/M IFA, no post-mortem	Suspected
2013	30F	Musina, Limpopo (from Zimbabwe)	Dog	Unknown	None	Abnormal behaviour, hyper- salivation, periods of aggres- sive behaviour alternating with calmness and seizures, healed scars behind left knee	Death	Post-mortem saliva - no post-mortem	Probable

*Age is given in years; M=male; F=female.

¹Classification of clinical cases according to the WHO Recommended Surveillance Standards, WHO/CDS/CSR/ISR/99.2

Conclusions

Rabies is a preventable but fatal neurological disease of humans and other mammals. Despite the availability of effective interventions for the control and prevention of this disease, cases of human rabies are confirmed in South Africa annually. In the past ten years, rabies has been reported from localities where it was previously controlled highlighting the fact that South Africa should be considered as an endemic site for rabies and that all exposures to suspected animals should be adequately assessed for risk of rabies. Low awareness of the risk of transmission of rabies virus after exposures to suspected animals (however benign the exposure may appear,

i.e. small scratches or licks on mucous membranes) in the general public but also in healthcare workers remains an important contributing factor in the failure of interventions to prevent rabies infection in human patients.

Acknowledgements

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