Profile of children with rabies dog bites: Manado experience, Indonesia

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Abstract

***Background*: Rabies is an infectious viral disease that is almost always fatal following the onset of clinical signs. Forty percent of all human rabies occur in children <14-year-old. In up to 99% of rabies virus is transmitted by dogs.**

***Objective*: To determine the mortality risk factor of children with rabies dog bites in Prof. Dr. RD Kandou Hospital, Manado, from 2012-2016.**

***Methods*: We performed a retrospective cohort study of all pediatric patients with rabies dog bites. Rabies was diagnosed via detection of nucleoprotein from dogs brain using fluorescent antibody test (FAT). We used chi-square test and calculated odd ratio using software SPSS 23.0 to determine the mortality risk factor of patients with rabies dog bites, considering p value <0.05 as significant.**

***Results*: During the study period, 38 children came with rabies dog bites (71.1% were boys). Incubation period range from 1 week to 4 years. Most common bites location was hand. Symptoms associated with rabies mortality were hydrophobia (OR 143, 95% CI 11.78-1735.96, p=0.0001), photophobia (OR 19.6, 95% CI 2.04-181.93, p=0.002), and hypersalivation (100% mortality, p=0.0001). Post-exposure vaccination associated with mortality of patients (OR 0.003, 95% CI 0.000-0.056, p=0.0001).**

***Conclusion*: Hypersalivation, hydrophobia, and photophobia are major risk factors of rabies dog bites mortality. Post-exposure vaccination is important to prevent rabies infection after a high-risk bite.**

Keywords: Dog bites, rabies, profile, children, Indonesia.

Introduction

Rabies is a deadly viral disease that is transmitted to human mainly by rabies dog bites. Rabies can be spread by animals such as dogs, wolves, cats, bats, monkeys, and also among humans. Rabies in humans has been eradicated in some developed countries, but can still be found in other countries including South East Asia countries. (1,2) Forty percent of all rabies cases in human occur in children. (3)

Up until 2015, high numbers of rabies cases were reported in 25 provinces of Indonesia, and 80,403 of those cases involved rabies-infected animal bites. Most cases were reported in Bali with 42,630 cases, followed by East Nusa Tenggara with 7,386 cases. Rabies-related deaths were 118. Most rabies-related death occurred in North Sulawesi with 28 cases and in Bali with 15 cases. (4)

Incubation period of rabies vary from less than one week to longer than one year (average 1-2 months), depending on the wound severity, bite locations, and the distance of the bite from the brain. (5) In most cases, rabies in human can be diagnosed from the clinical symptoms, medical history or dog bite scars/wounds, the dead animals that bit the patients, and incomplete post-exposure vaccination. The symptoms of rabies include

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changes of the sensory perception, fever, excitability, anxiety, aerophobia, hydrophobia, hypersalivation, and convulsion (rabies encephalitic). In 20% of the cases, rabies paralytic may occur. In rabies paralytic, the muscles can paralysis slowly, starting from the bite location. (5-7) The gold standard for rabies test is through the detection of Negri bodies from the brain, although positive results are less than 80%. Non-detection of Negri bodies does not lower rabies risks.

From the clinical rabies development, factors such as the degree level of wounds, virus proportion of rabid dogs, and pathogenicity of the virus can affect the outcome of children infected with rabies. Without clinical treatment, death often occurs two to six days after clinical symptoms are observed. The highest level of infection causing mortality is from the bites on the face. The midlevel of infection is from the bites on the arms and hands while the lowest level is from the bites on the legs and feet. Death is commonly caused by respiratory failure. (8,9)

The goal of this research was to determine the mortality risk factor of children with rabies dog bites at Prof. Dr. RD Kandou General Hospital Manado.

Methods

A retrospective cohort study was conducted at Prof. Dr. RD Kandou General Hospital Manado from January 2012 to December 2016. Inclusion criteria were children <18 years of age with rabies dog bites. Rabies was diagnosed with detection of nucleoprotein from dog brains with fluorescent antibody test (FAT) by Veterinary Research, Department of Agriculture. Exclusion criteria were medical history with neurologic disorder, seizure disorders. Data was collected from medical record of Department of Pediatrics, Prof. Dr. RD Kandou General Hospital, Faculty of Medicine, Sam Ratulangi University.

This research studied children who died from or have survived rabies dog bite, and data from the time the patient had been bitten by rabid dogs until rabies symptoms appeared were gathered. Data obtained were characteristics of patient, incubation period, symptoms related to the mortality outcome, and outcome of post-exposure vaccination. Patients' analyzes were age, gender, location of bite, and length of hospitalization. Symptoms such as fever, convulsion, hydrophobia, photophobia, hypersalivation, post-exposure vaccination were related to the mortality outcome of patients.

The data were statistically analyzed using computer software SPSS 23.0. To analyze the association between risk factors and human rabies mortality, we used Chi-square test. $p<0,05$ indicated statistically significant, and calculated odd ratio (95% CI) for human rabies mortality risk factors. Risk factors were bite location, incubation period, fever, and convulsion. Symptoms related to the mortality rates from rabies were hydrophobia, photophobia, hypersalivation, and post-exposure vaccination.

This research has been approved by Research Ethical Committee and Health Development of Prof. Dr. RD Kandou General Hospital with reference number PP.061/V/Dik/2017.

Results

Thirty-eight children were admitted with rabid dog bites in January 2012 - December 2016. Bites were most common at the age of ≤5-year-old (52.6%) and 71.1% were boys. The incubation period varies from one week to four years. The most common incubation period was ≤2 weeks (42.1%). The most common location for the bites was the hand with 34.2%. The length of hospitalization of <2 days was 47.4%, and 39.5% from those experienced death (**Table 1**).

Symptoms related to the mortality from rabies were hydrophobia (OR 143, 95% CI 11.78-1735.96, p=0.0001), photophobia (OR 19.6, 95% CI 2.04-181.93, p=0.002), and hypersalivation (100% mortality, p=0.0001). Post-exposure vaccination had a protective factor toward the mortality of children with rabid dog bites (OR 0.003, 95% CI 0.000-0.056, p=0.0001) (**Table 2**).

Discussion

Rabies is a viral disease which causes acute encephalitis by the genus Lyssavirus, family Rhabdoviridae. Infections are commonly caused by bites and scratches from rabies animals. This virus attacks central nervous system, causing progressive paralysis, encephalitis, and coma. Once symptoms develop, rabies can be fatal. (5,8,10-12)

In this research, children with male gender and less than 5 years of age were the most common victims of the bites from rabid dogs. This observation supports research findings by Seligsohn that showed boys are the most common victims of rabies because boys are often engaged in unsafe behaviors than girls. (13,14) A study from Yibrah M. et al in Ethiophia (2015) observed that the majority (62.8%) of the rabies cases were among males. This might be explained by the activities males frequently involve in: they might do more nightly and outdoor activities while females are more likely to remain indoors due to cultural and religious reasons. A large proportion human rabies exposure cases

were reported among children under 15 years of age (38.5%). This could potentially be explained by the fact that children are more likely to provoke dogs and are also less likely to be able to defend themselves, thereby being more exposed to dog bite injuries. (10)

The incubation periods in this research ranged from one week to four years; most common incubation period is ≤2 weeks (42.1%). More than 50% of children who died have an incubation period of less than one month. The incubation period of rabies virus can be shorter for deep bites, bites on face, head, and hands, and multiple symptoms. For bites on head, face, and neck, the incubation period is 30 days while the incubation period for bites on the arms, hands, and fingers is 40 days. When bitten on the legs, feet, and toes, the incubation period is 60 days. The incubation period for bites on the body is approximately 45 days. (15-17)

The most common location for the bites in this study was hand (34.2%). Tenzin et al found that the face, neck, and head were the most common locations for the bites (more than 70%). These observations depended upon whether the dogs were pets or strays. Pets often bite on the face, head, and neck because of the short height of children and the playful interactions between the dogs and children such as hugging and licking. On the other hand, stray dogs often bite the extremities of children. Children are also often used hands and feet to bother stray dogs and protect themselves from attacks. (16,17)

Mortality risks from rabies dog bites from reported cases were 45% for bites on head, 28% for bites on hand, 5% for bites on body, and 5% for bites on feet. Tenzin et al suggested that mortality rates went up 19.24 times each year without post-exposure vaccination in Bhutan, equivalent to 40 deaths in 100,000 populations per year. (13)

The early symptoms of rabies are similar to other systemic virus infections such as fever, headache, malaise, upper respiratory disorder, and gastrointestinal disorder. After inoculation, virus binds to nicotinic acetylcholine receptors at neuromuscular junction. The rabies virus progresses from the subcutaneous tissue or muscle into peripheral nerves. The virus then migrates along nerve to the spinal cord and brain via retrograde fast axonal transport, repiclate in motor neurons of the spinal cord and local dorsal root ganglia and rapid ascent to brain. The children exhibit behavioral changes and clinical signs when the virus reaches the brain. After reaching the central nervous system, rabies virus causes acute and progressive encephalomyelitis that is proved to be fatal. The virus then travels into the salivary gland. There are two different symptoms of rabies. The most common form is furious (encephalitic) with symptoms of hydrophobia that can quickly develop into encephalitis and death. The other form, paralytic, seldom occurs, but that can develop into progressive flaccid paralysis. (5,6)

Hydrophobia and aerophobia are presented when patients were asked to drink water and when air was blown to the face of the patients. The desire to swallow liquids and fear, along with pharynx and larynx muscles spasms, can cause aspiration of liquid into the trachea. Hydrophobia occurs because of muscle spasms caused by the damage of nucleus ambiguus which controls inspiration. (2,8) Painful spasm develop in the muscles that control breathing and swallowing. The individual may begin to drool thick saliva (hypersalivation). Photophobia and convulsion occur as symptoms from rabies encephalitis. A study by Muyila DI et al (2014) showed that clinical features of 21 children with rabies at admission were fever 71.4%, hydrophobia 90.5%, and hypersalivation 52.4%. (18)

Symptoms related to the mortality for rabies are hydrophobia, photophobia, and hypersalivation. Hydrophobia can increase mortality risk by 143 times for children with rabies dog bites. Photophobia increases mortality risk by 19.6 times while hypersalivation is related to 100% mortality. Hydrophobia, photophobia, and hypersalivation are recognized as the pathognomonic symptoms for rabies.

Cleaning the wound is an important step in the treatment of rabies-infected animal bite cases. The bite wound needs to be cleaned with running water and soap for 10-15 minutes. After cleaning the bite wound, antiseptic agents such as 70% alcohol can be applied. The bite wound should not be sewn in order to reduce viral invasion of the wound. The administration of anti-rabies vaccine and anti-rabies serum is determined based on the category of bite wounds and the conditions of the biting animal. Patients with high-risk wounds must be given anti-rabies vaccine and serum. Post-exposure vaccination must be administered promptly for all patients bitten by rabies dogs. (4)

Rabies is a fatal disease in humans, and, to date, the only survivors of the disease have received rabies vaccine before the onset of illness. No single therapeutic agent is likely to be efective, but a combination of specific therapies could be considered, including rabies vaccine, rabies immunoglobulin, monoclonal antibodies, ribavirin, interferon-α, and ketamine. (19) A report from Huang et al (2017) showed that rabies is preventable using effective measures including immediate wound washing vac-

cine therapy, and wound infiltration with rabies immunoglobulin. (20)

Early diagnosis of rabies in dogs and other animals is crucial for the basis of post-exposure vaccination for children to prevent rabies. The rabies virus can stay in the muscle tissue for long periods and in certain circumstances, and its long persistence may provide an opportunity for host immune clearance and post-exposure treatment. Post-exposure vaccination (from purified cell-culture and embryonated egg) with good wound care and immunoglobulin anti-rabies injection are the most effective treatment to prevent rabies in children, although high risk exposure. We found that post-exposure vaccination for rabies bites has protective factor against mortality in children with rabies dog bites. Children with rabies dog bites need five dosage of rabies vaccine for effective treatment. However, most of the rabies patients do not receive rabies vaccine, and if vaccine is administered, the full dosage is not complete. Of the fifteen children who died, only one child received post-exposure vaccination. From anamnesis obtained, the child only gets one vaccination and there was unavailability of immunoglobulin in that area. In the 2004 survey only 39.5% of patients cleaned the wound from the bites with water and soap and 46.9% received the rabies vaccine. (21-27)

Conclusion

Hypersalivation, hydrophobia, and photophobia are major risk factor of rabies dog bites mortality. Post-exposure vaccination is important to prevent rabies infection after a high-risk bite.

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Competing interests

The authors declare that they have no competing interests.

Table 1. Characteristics of children with rabies dog bites

Characteristics	N (%)	
	Survived (n=23)	Died (n=15)
Age (n=38)		
- ≤5 years	13 (34.2)	7 (18.4)
- >5-≤10 years	9 (23.7)	6 (15.7)
- >10 years	1 (2.6)	2 (5.2)
Gender (n=38)		
- Male	15 (39.5)	12 (31.6)
- Female	8 (21)	3 (7.9)
Incubation period (n=38)		
- ≤2 weeks	13 (34.2)	3 (7.9)
- >2 weeks-≤1 month	4 (10.5)	6 (15.8)
- >1month-1 year	4 (10.5)	6 (15.8)
- >1-≤4 years	2 (5.3)	0 (0)
Location of bites (n=38)		
- Head	3 (7.9)	8 (21)
- Hand	9 (23.7)	4 (10.5)
- Leg	6 (15.8)	3 (7.9)
- Other locations	5 (13.2)	0 (0)
Length of hospitalization (n=38)		
- <2 days	3 (7.9)	15 (39.5)
- 2-4 days	5 (13.1)	0 (0)
- >4 days	15 (39.5)	0 (0)

Table 2. Mortality risk factor in children with rabies dog bites

Variable	Died N (%)	Odd Ratio (95% CI)	p value
Fever (n=30)	13 (43.3%)	2.29 (0.396-13.28)	0.346
Convulsion (n=8)	5 (62.5%)	3.33 (0.660-16.85)	0.134
Hydrophobia (n=14)	13 (92.9%)	143 (11.78-1735.94)	0.0001
Photophobia (n=8)	7 (87.5%)	19.6 (2.04-181.93)	0.002
Hypersalivation (n=13)	13 (100%)	UN	0.0001
Post-exposure vaccination (n=15)	1 (4.35%)	0.003 (0.000-0.056)	0.0001

Legend: UN=undefined.

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