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Case Report

Leptospirosis: an Overview of Canine Leptospirosis in Grenada and Its Impact on Public Health

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Abstract

Leptospirosis is a zoonotic disease that cans cause severe disease manifestation in humans and as such, is considered a public health threat. The *Leptospira* bacteria are quite prevalent in warm, tropical regions including the island of Grenada. The spread of this disease in Grenada's canine population can be curbed with the use of an efficient prophylactic measure; however, the efficacy of Leptospirosis vaccines is questioned. The current vaccine distributed to Grenada from the US and Europe contains serovars Grippotyphosa, Canicola, Icterohaemorrhagiae RGA and Pomona. A 2005 study in Grenada, however, revealed serovars Copenhageni, Mankarso, Icterohaemorrhagiae RGA and Pyrogenes to be present in the local environment which suggests little cross-protection offered to dogs that have been vaccinated. Detecting Leptospirosis spill over into the human population is difficult due to non-specific symptoms as well as poor physician awareness. Recommendations to amend and address this public health threat in Grenada are discussed.

Introduction

Leptospirosis is a neglected tropical disease that is infectious and zoonotic in nature. It is caused by the pathogenic spirochete, *Leptospira interrogans*, which is prevalent in warm, tropical regions worldwide, including Grenada [1]. The disease causing agent is particularly found in large stagnant bodies of water, muddy puddles, moist soil and in the urine of infected animals such as cattle, swine, rats and dogs which all serve as reservoirs for the disease. Transmission can occur directly through contact of mucosal membranes and broken skin between *Leptospira* contaminated soil, water or urine or indirectly through the environment. General pathogenesis involves *Leptospira* infecting the bloodstream where it then travels to attack multiple body systems including the brain, heart, lungs, liver and finally settling in the kidneys to proliferate and be excreted in the urine in large quantities [2,3].

Rats are primarily implicated for the spread of Leptospirosis due to their extremely pervasive presence in the environment. In fact, a 2009 study conducted in Grenada confirmed that of the 237 serum samples tested belonging to rodents of the Rattusnorvegicus group, there was a significant seroprevalence of 27% with identified serovars predominantly of the Icterohaemorrhagiae serogroup [4]. Sanitation and human behavioral risks are also strongly considered towards disease transmission as research suggests complex environmental issues, such as those found in Grenada, as contributory factors [5]. However, stray dog population [6] in Grenada along with the growing bond between humans and dogs create a mounting concern due to increased risk of exposure resulting in a human case fatality rate between 5% to 70% [7]. According to [8], access to diagnostic tools, socioeconomic status, population structure, life expectancy at birth, distance from the equator, tropical island, and urbanization have all been accounted as factors contributing to the wide range in case fatality rate. In its early stages, Leptospirosis in dogs and humans presents with nonspecific symptoms including but not limited to fever, lethargy, muscle aches, decreased appetite, skin rash (humans), conjunctivitis, and vomiting [2]. In its more advanced stage, the disease presents with jaundice, kidney failure, pulmonary disease, and edema in dogs and kidney degeneration, jaundice, meningitis and pulmonary hemorrhagic syndrome in humans [9,10]. The nonspecific symptoms in humans often mimic the flu while the advanced stages are said to mimic Dengue hemorrhagic fever, contributing to the misdiagnosis and underreporting

of Leptospirosis worldwide [11].

As a result, particular attention must be paid to the efficacy of cross protection in canine vaccines against local circulating disease causing *Leptospira* serovars in an effort to assess the efficacy of the vaccine in curbing canine exposure and zoonotic transmission. Additionally, keen awareness of disease symptoms and pathogenesis in humans must be developed among physicians in order to help combat this growing public health threat.

Disease Background

Annually, the world sees an estimated 1.03 million cases of Leptospirosis in addition to 58, 900 human deaths [12] and figures are expected to rise owing to climate change and rapid urbanization [13]. However, due to the manner of symptom manifestation as well as the lack of proper diagnostic tools in developing countries, the statistics may not accurately reflect the true disease prevalence. Because high disease prevalence results in economic burden, especially in developing regions such as Grenada, it is critical to consider as many methods of prevention as possible to curb the rate of zoonotic transmission. Theoretically, one identifiable way to reduce human exposure to Leptospirosis is to target the risks of exposure from dogs by preventing their own exposure to *Leptospira* using vaccine protocol.

Globally, there are over 250 circulating *Leptospira* serovar types and of those types only four are included in current canine vaccines that are globally distributed from the U.S. and Europe [14-16]. Studies suggest that canine leptospirosis is traditionally caused by Grippotyphosa, Canicola, Icterohaemorrhagiae RGA and Pomona and these specific serovars are currently found in European and American distributed vaccines [17]. The challenge of the vaccine's efficacy stems from the fact that it may not offer cross protection due to a variety of region specific circulating servovars [17]. According to [18], immunity to Leptospirosis is serovar specific which is why knowledge of serovars that commonly cause disease within a particular geographic region is important for vaccine development and efficacy.

Leptospira Epidemiology in Grenada and Neighboring Countries

The threat of Leptospirosis to public health is relevant in Grenada as it satisfies the epidemiological triad of agent (*leptospira*), environment (Tropical Climate) and reservoir (Dogs). Moreover, Grenada's status as a developing country adds to its vulnerability since it lacks disease awareness and capacity to properly diagnose and manage Leptospirosis as well as to keep a firm handle on the stray dog population [6,19]. As a result of this significance, a study was conducted on the island in 2005 to begin the assessment of local circulating serovars in the canine population as well as to assess any cross-protection provided by associated vaccines [20]. Diagnostic tests of the dogs sampled in the study revealed seroprevalence rates between36.1% to 93.3% from the Enzyme-Linked Immunosorbent Assay (ELISA) while the most prominent circulating serovars identified were Copenhageni, Mankarso, Icterohaemorrhagiae RGA and Pyrogenes based on the Microscopic Agglutination Test (MAT). Referring back to the Clinician's Brief 2013 report on the current serovars included in the canine vaccine distributed by the US and Europe, it is evident that little to no cross-protection would be offered which limits efficacy and does nothing to reduce exposure in the vaccinated canine population in Grenada.

While surveying neighboring developing nations in the West Indies, data gathered in Trinidad determined the top four circulating serovars as Mankarso, Icterohaemorrhagiae RGA, Autumnal is, and Copenhageni [21].According to approximately 50% of surveyed healthy seropositive dogs had history of Leptospirosis vaccination which indicates a lack of cross protection and overall vaccine deficiency due to differences in vaccine serovars and environmental serovars.

Furthermore, the study reports that of canine blood samples collected and tested in 2005, an estimated seroprevalence of 4.4% was detected in stray dogs infected with *leptospira*. This percentage starkly contrasts that of what was discovered only two years later in Trinidad, with seroprevalence soaring to 15.5% [22].Though this sharp increase in such a short period could accurately reflect the true rise in prevalence, the increase could also be due to the difference in antigen panels that were used in both studies. Based on these findings in Trinidad, it would be interesting to see the current *leptospira* seroprevalence in Grenada for the sake of surveillance as well as to further cement the fact that more attention must be paid towards poor vaccine cross-protection in inoculated dogs and the impact that has on public health on the island.

Despite the abundance of outdated data pertaining to the prevalence of canine Leptospirosis in and around Grenada, many countries surrounding the island suggest that the disease is more of an occupational one that can be prevented with the use of traditional methods. Jamaica is one such country that suggests that hand washing and proper use of personal protective gear while engaging in occupational activities such as butchering and forestry will curb disease transmission as opposed to focusing on the underlying causes discussed above [23].

Vaccines against Canine Leptospirosis

The case for potential vaccine deficiency in Grenadian dogs is supported by studies conducted in other countries that highlight this issue with regards to cross-protection, short duration immunity and even severe adverse reactions. The standard Leptospirosis vaccine is created via whole-cell preparations with leptospiral lipopolysaccharides and residual medium components which have

been implicated for short-term immunity and adverse reactions reported in dogs [24,25]. The vaccine is also serovar specific which, again, does not lend to adequate protection in regions that have *leptospira* strains different from what is found in vaccines therefore creating a challenge in successfully creating a vaccine that provides adequate coverage in canines.

Conducted a study in which hamsters were tested with a *Leptospirosis* vaccine containing a recombinant LipL32 antigen (a protein expressed in all pathogenic leptospira species) and rLTB (B subunit of the Escherichia coli heat-labile enter toxin) [24]. Results from that study were promising in that while protection against other serovars still needed to be addressed, high immunogenicity was reached with a potential for replacing tradition Leptospirosis vaccines once optimum dose and other vaccine dynamics were established. As previously mentioned, issues with cross-protection, specifically in Grenada, due to dissimilar serovars found in vaccines compared to that in the environment is cause for concern, especially with very little regional research conducted. There is, however, an abundance of data available on the adequacy and inadequacy of leptospirosis vaccines in Europe and the US where vaccine manufacturing occurs.

Recent research conducted in Europe suggested that vaccines should specifically target sero groups Canicola, Icterohaemorrhagiae, Grippotyphosa and Australis [26] while multiple studies conducted on behalf of the European Pharmacopoeia suggest that a new vaccine containing Canicola, Icterohaemorrhagiae, Bratislava and Grippotyphosais effective at offering cross-protection in canines tested within that region. The point being made is that, like Europe, if there was sufficient data available in Grenada and in the surrounding regions highlighting the need for more effective prophylactic measures then more attention would be paid to making substantial attempts at curbing transmission between dogs and humans on the island [27].

Physician Awareness and Human Implications

Reported clinical human cases of Leptospirosis in Grenada along with research to support its occurrence in the human population is few and far between as little to no current data regarding the prevalence or incidence of human infection can be found. This is not to suggest that cases are not suspected or at least documented, however. In 2011, a 9-year study from 1997-2005 was published on the epidemiology of Leptospirosis in the Caribbean which showed that of 14 countries sampled for seroprevalence with the use of human serum, Grenada was fourth in demonstrating frequency of seropositivity [28].

Keeping in mind the diagnostic tools used in that study, what was detected may have been an underestimate of the true occurrence in humans. The study also reinforced the fact that *Leptospirosis* can manifest synonymously to that of Dengue Hemorrhagic Fever, which may cause for skewed results. Also mentioned was the identification of the most common serovars in the Caribbean environment, *Copenhageni* and *Icterohaemorrhagiae*, which again highlights the stark contrast between seroprevalence in the Caribbean and Europe, where most vaccine production occurs.

Essentially, Grenadian physicians and other health care professionals need to be cognizant of Leptospirosis' threat to public health regardless of the lack of current data. Health care professionals should have a firm grip of disease transmission and clinical manifestation in order to treat early, compress morbidity and prevent death. Furthermore, Grenada along with its neighboring West Indian countries should develop a system wherein rapid and reliable diagnostic services can be made available to aid in differential diagnosis between the flu, Dengue Hemorrhagic Fever and Leptospirosis for the sake of proper surveillance.

Conclusion

Due to Grenada's inadequate data available on prevalence of Leptospirosis in the canine and human population, it is critical that physicians develop an enhancement in their level of awareness, acknowledgement and understanding of the disease as it pertains to its presence in the environment, its reservoirs as well as the clinical manifestation in humans. Physicians in Grenada must stay abreast of information concerning diseases that plague tropical regions and if no such information exists, they should take the initiative to mobilize a surveillance system for the sake of public health.

Likewise, veterinarians in Grenada and neighboring countries must be aware of the constant shifts in *leptospira* serovars that circulate region to region as well as appreciate the negative impact on canine and human health from having little to no cross-protection from Leptospirosis vaccines. As such, it is recommended that the Caribbean region develop its own *leptospira* surveillance system in conjunction with canine vaccine development capabilities targeted specifically towards local serovar types with the purpose of ensuring proper cross-protection and long term immunity in the canine population as an effective way to mitigate Leptospirosis as a public health threat.

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