**Literature Review on the Transmission, Management, and Prevention of Rabies Outbreaks in Kazakhstan**

Rabies is a viral and zoonotic disease, meaning that it is an infectious disease that is transmitted between animal and human species. Rabies is present on all continents; however, primarily targets poor communities living in remote locations. Rabies is a deadly disease if left untreated. Dogs are identified as the main source of transmission cases to humans. The most common method of transmission is saliva, which occurs during bite and scratch incidents. The incubation period of rabies is around 3 months, yet the time may vary depending on the location of virus entry. The rabies virus causes inflammation of the central nervous system, specifically fatally targeting the brain and the spinal cord. The two forms of diseases are furious and paralytic rabies. Furious rabies cause hyperactivity, hydrophobia, and aerophobia and result in proximal death due to cardio-respiratory arrest. Paralytic rabies, which is the less common form of the disease, cause muscle paralysis and development of a coma, which causes misdiagnosis and under-reporting of the disease. (1)

Kazakhstan is a landlocked country in Central Asia that is known as the ninth largest country in the world. Kazakhstan’s abundance of natural mineral resources and arable land has historically been exploited by the corrupt Kazakhstani government as well as envious outside countries. A little over half of the population lives in urban cities, while others are scattered throughout various regions of the country living in very segregated and poor conditions. The rates of infant and maternal mortality, life expectancy, and healthcare standards in Kazakhstan are much lower than those in the Western hemisphere. Healthcare is provided free of charge for all people; however, medical facilities are centralized in urban towns leaving many provincial regions with insufficient health resources. (2)

Rabies is one of Kazakhstan’s current epidemiological issues, which contributes to the topic of human development. Amartya Sen describes human development as the expansion of human freedoms (3). Prevention and management of rabies outbreaks relates to his definition by virtue of expanding human freedoms through elimination of a disease. Disease is a debilitating factor present in human lives, so elimination of rabies, in both animals and people, would create a better living space for humanity as a whole. Getting bitten by an animal and fearing the transmission of rabies is a palpable fear of Kazakhstani people because of the massive numbers of stray animals roaming the streets. Not only would people be able to live a more free and healthier lifestyle, but prevention of rabies would limit human mortality which is an immediate limitation on human freedom. Furthermore, economic, physical and time resources are required to address a rabies outbreak; therefore, in the absence of the disease, people could choose where to supply those resources. Funds used to combat rabies can be used towards a better cause, such as improvement of Kazakhstan’s economic situation.

The authors use a variety of methods to assess and model the rabies epidemiological processes in Kazakhstan. Mukhanbetkalyev et al. use data to model cluster zoning of outbreaks throughout the country (4). The datasets used by the authors include epidemiologic information about each occurred outbreak of rabies and anthrax, provided by veterinary research institutions and laboratories throughout Kazakhstan (4). The authors use the concept of a basic reproductive ratio to simulate the possibility of new rabies outbreaks (4). Other researchers - Abdrakhmanov et al. - use a maximum entropy modelling method for their gathered data to develop a geospatial regression model between rabies outbreaks and a set of climactic, geographical, and ecological factors as explanatory variables to identify the risk of rabies outbreaks in Kazakhstan (5). To conduct their research, the authors use 2003-2014 rabies outbreak data provided by the Kazakhstani veterinary services, which includes 762 cases of rabies outbreaks in domestic, wild, and farm livestock animals (5). The authors also use temperature, precipitation and altitude datasets from WorldClim, as well as green vegetation fraction and land coverage data provided by the United States Geological Survey (5). Grigoryan et al, another group of rabies researchers, gather data to perform a descriptive epidemiological analysis based on the review of retrospective and operative information about the occurrence of human rabies in the Former Soviet Union republics (6). The authors use data sets containing the number of animal bite instances, number of executed post-exposure prophylaxis treatments, and the mortality rate for various Former Soviet Union countries (6). Sultanov et al. too conduct research on rabies: they analyze gathered data through GIS technology to illustrate the density estimation for animal rabies on the map of Kazakhstan, as well as the density estimation for outbreaks of rabies (7). The scientists use public health and veterinary surveillance data from 2003 to 2015, diagnostic results provided by the regional branches of the Republican Veterinary Laboratory, as well as statistical data from the Ministry of Agriculture, Veterinary Control, and Monitoring Committee (7). For human rabies data, the number of individuals with animal bites and those who received the post exposure prophylaxis was provided by the Kazakhstani government’s monitoring committee (7).

Rabies are identified to be an infectious disease that spreads from animal species to other animals or humans. One research study finds that most rabies cases occurring amongst farm animals are cattle, amongst domestic animals are dogs, and amongst wild animals are foxes (4). The researchers also identify rabies as an epidemic of secondary nature in domestic animals since it is found to mostly be transmitted through contact with wild/stray animals (4). A group of researchers find the correlation between the number of rabies diseased cattle and the number of sick dogs and cats in the same area to be about 70% (8). The correlation between the number of diseased cattle and wild animals, however, was only around 15%, indicating that stray dogs and cats are the more likely transmitters of rabies to cattle (8). When other researchers conduct a study to see where rabies is most prevalent geographically, they identify areas alongside Kazakhstan borders to be the most prone to rabies outbreaks (5). The largest clusters are located in Western Kazakhstan, specifically Kostanay and Zhambyl regions (8). This may suggest a possibility of disease importation from abroad. Animals, especially the wild species, move independently and can easily interact with those across administrative borders where rabies laws and regulations can be different. However, it’s also important to note that the land alongside borders naturally has a higher rate of inhabitation of both animal and human species, possibly explaining the increased transmission of rabies (5).

One of the most common prevention methods against rabies is animal vaccinations. The current program imposes mandatory vaccination policies for all susceptible livestock in high risk areas and monitoring practices in all other areas. Though most vaccinations occur orally, some animals get vaccinated through consuming baits placed throughout the woods (7). Kazakhstan had eradicated foot and mouth disease, another zoonotic type of infection, by 2013 through the strategy of animal vaccination (4). The government tried to replicate the same vaccine approach for rabies; however, the method did not prove to be efficient (4). The current measures imposed by the Kazakhstani government against rabies are oral vaccinations of animals in areas with an active outbreak as well as adjacent territories, forced preventative vaccination of animal species prone to rabies, control of stray animals, and various awareness raising campaigns (5). One group of researchers finds no discrepancy between the suggested vaccination standards and the actual vaccination percentages amongst farm and wild animals, indicating the ineffectiveness of the oral vaccination process (4). However, other researchers find that one of the two currently administered vaccines, the Indian Raksharab, is ineffective in antibody production against rabies (7).

Although not commonly-used in Kazakhstan, there are a plethora of diagnostic testing methods that exist for accurate detection of the presence of rabies in a human body. Hemi-nested polymerase chain reaction (RT-hnPCR) has been proven to be an efficient method of diagnosing rabies in humans (9). However, other researchers clarify that such reagents and kits are not readily available at medical centers throughout many rabies-affected countries due to the associated costs (6). A lot of former Soviet Union countries don’t have the means of producing

treatment shots on their own and, therefore, must turn to importation of pharmaceuticals. Some testing can also be performed post-mortem, which is known as the fluorescent antibody test (FAT) (9). The test examines a brain sample for the virus antigen, but is different from necropsy, and therefore can be accepted by more communities due to the absence of religious conflicts surrounding necropsy (6). Although expensive, diagnostic testing allows for accurate detection and management of rabies but can also provide transparent data about the epidemiological situation in Kazakhstan.

The most common form of rabies treatment is post-exposure prophylaxis (PEP), which is administered in a series of treatment shots. Some researchers believe this use of the treatment medication is highly wasteful as not all animal bites automatically equate to a transmission of rabies (6). Moreover, unnecessary administrations of the shots can lead to a shortage in a critical scenario (6). On the other hand, the authors explain that many people, typically those from poor villages, who are naturally at high risk of rabies transmission, do not live in close proximity to medical centers, and therefore are unable to receive treatment (6). Post exposure treatment is the biggest contributor to the annual total loss from rabies, which Sultanov et al. evaluate at $20.9 million annually (7). Categories that contribute to the annual total cost, from most to least financially impactful, were identified as follows: post exposure prophylaxis treatment, death and its associated costs, animal control, vaccination of domestic animals, vaccination of wild animals, and livestock loss (7). Though the post exposure prophylaxis is a major cost, it has proven to be one of the most effective tactics when combating rabies.

Researchers conclude that the number of bite incidents has been rising over the years, alongside the increased administration of the post exposure prophylaxis treatment (7). Other researchers link the increased number of cases to the worsened winter conditions in Kazakhstan (8). They explain that the lack of natural food sources brings wild and stray animals to farms where they transmit rabies to cattle (8). Children between ages of 6-14 years old are identified as the age group that is most likely to get bitten by animals (7). The authors also conclude that bites in different parts of the body carry different probabilities of rabies transmission (7). Similarly, they are able to identify a pattern showing that lower extremities are the body part most susceptible to bites. Other researchers note an interesting pattern that the number of individuals who received rabies from a bite is lower than the number of reported rabies cases, indicating that rabid animals tend to bite multiple times (1). Their study shows that almost all cases of human rabies were seen in individuals who did not receive the post exposure prophylaxis shot treatment (1).

Researchers have proposed multiple potential solutions to help combat rabies in Kazakhstan. One proposed solution is providing the rabies shots free of charge to those who financially cannot afford it (6). Although there is free healthcare in Kazakhstan, it is inefficiently run to where costs associated with transportation and medication can stand in the way of people getting access to the post exposure prophylaxis shots. Other researchers suggest a modification of the current vaccination program since they have not been able to prove its effectiveness (7). Sultanov et al. discuss the benefits of stopping livestock vaccination in order to use the funds for vaccinations of dogs and foxes (7). The researchers suggest that this would indirectly protect the livestock and create new funding that can be used towards control of stray animals (7). Stray dogs happen to be a massive problem in Kazakhstan that pose a significant rabies risk because of their difficult-to-track nature. Another group of researchers introduce the idea of oral vaccinations through a process similar to “catch-sterilization-release”, yet they recognize the difficulty of allocating the proper resources for the method (6). Grigoryan et al. too suggest development of a new vaccine; however, they recognize that the option is highly time and labor consuming (6). Another introduced solution is the government’s ability to prohibit people from feeding stray dogs in attempts to decrease reproduction (6). However, such practice may be viewed as too radical in the public view and may require prior awareness campaigns.

One group of researchers conclude their paper by stating that the current approach is inadequately allocating the country’s funds and is preventing further research from being conducted because of the lack of data available on rabies (6). The economic situation is not prosperous enough to be able to afford to test most of the proposed solutions because zoonotic diseases are relatively low-damage causing in the grand scheme of issues in Kazakhstan. The government is very poorly organized and lacks cohesion amongst the different departments (4). This makes it difficult to efficiently address a problem: especially one that requires combined efforts of various institutions. Zoonotic diseases carry a significant threat to both animals and humans, but the uncontrollable and difficult-to-trace transmission of such diseases takes a toll on the economy. Combating rabies is a complex task, specifically in Kazakhstan, because of the large number of stray animals that are left unaccounted for in statistics (5). Animal disease control centers are not focused on catching and fostering the animals which causes more complications. First, the stray animals are able to go wherever they choose, which increases their points of interaction with other animals, which in turn translates into increased risks of rabies transmission. Secondly, most stray animals have no shelter or food, which can cause them to behave aggressively and bite people. Each bite can potentially transmit rabies, but it also depletes the economy of the post exposure prophylaxis resources, which are valued at $147 per treatment (6).

In summary, the current research identifies rabies as a significant problem in Kazakhstan. Stray dogs are identified as the main transmitter of rabies (1). However, disease importation is another possible explanation (8). An intra vitam polymerase chain reaction test and a post mortem fluorescent antibody test have been identified as accurate diagnostic tests for rabies; however, the associated costs prevent them from being commonly used in Kazakhstan (9). Animal vaccinations are viewed as the most cost effective rabies prevention method, however, the current vaccination protocols must be changed to provide more results according to researchers (7). Post exposure prophylaxis treatment is an effective response technique in preventing transmission to humans; however, is the major contributor to the massive monetary losses from rabies incurred by Kazakhstan’s government (6). Some of the possible solutions include a modification of the current vaccination program, stricter control of stray animals, and development of a new vaccine (6,7). The rabies situation is also complicated by the lack of available data on the topic and the lack of collective effort to combat the disease from the government (4).

The available literature lacks more careful examination of the available diagnostic tests and their possible integration into rabies treatment protocols in Kazakhstan. The use of diagnostic testing could eliminate the overuse of the prophylaxis treatment. Further work could also include introduction of various other geographical and environmental variables into the zoning model.

The central research question of this investigation could be how do rabies outbreaks occur in Kazakhstan and what could be done to prevent them.

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