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Review Article

Prioritised Zoonotic Diseases of Nepal: A Review

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Abstract

World Organization for Animal Health (OIE) has estimated that 60% of infectious diseases and 75% of emerging and re-emerging diseases of humans have an animal origin. In Nepal there six zoonoses; Taeniasis/cysticercosis /Neurocysticercosis, Leptospirosis, Hydatidosis, Brucellosis; Toxoplasmosis and Avian Influenza are identified as priorities zoonotic diseases as they are found to have epidemic potential. Although they are prioritised, there is high prevalence of these diseases in both humans and animals with insufficient research and data. Coordination of multiple stakeholders of public and animal health and One Health collaboration are crucial to control and elimination zoonotic diseases in Nepal.

Keywords: Animal Health; Public Health; One Health; Veterinarians; Zoonosis

Introduction

Zoonosis are those infectious diseases that are naturally transmitted between human and vertebrate animals (Slingenbergh *et al.*, 2004).Over the past ten years most (about 75%) of the new diseases which infect humans are caused by animal or animal product originating pathogens (Chomel *et al.*, 2007). Zoonotic diseases may be bacterial, viral, parasitic, protozoal, and fungal or may involve unconventional agents which may cause many types of illnesses in both human and animals that range from mild to serious and even death. Animals which seem to be healthy are also carrying germs sometimes that can cause illness in human, depending on the zoonotic disease(Slifko *et al.*, 2000). The bonding between humans and animals have been seen for many years, and pet ownership has been associated with both emotional and health benefits, but pet ownership may also have some health risks through the zoonotic transmission of infectious diseases (Grant and Olsen, 1999). Identifying wild reservoirs of zoonotic pathogens is really prioritized in public health as each year over 1 billion cases of human illness attributable to zoonoticdisease(Han *et al.*, 2015). The number of zoonotic disease that originate from wild animals in particular has increased substantially in the past few decades, even in the wake of increased reports of new emerging infectious diseases(Pavlin *et al.*, 2009).

Zoonotic diseases are basically of three groups; endemic, epidemic and emerging. Endemic zoonotic diseases are present in many portions of the globe and affect large group of human and animal population. Epidemic zoonotic diseases are scattered and patchy in the occurrence whereas the emerging zoonotic diseases are those diseases whose incidence are increasing rapidly across the globe, and these disease maybe new or may have occurred in the past(Maudlin *et al.*, 2009).In the least developed countries of the world, around 20% of all human morbidity and mortality are attributable to endemic zoonoses(Elelu *et al.*, 2019).Anthrax, bovine tuberculosis, brucellosis, cysticercosis, echinococcosis, leishmaniasis, rabies and human African trypanosomiasis are eight diseases identified by WHO as neglected zoonotic diseases (NZD) (Adhikari and Bagale, 2019). NZD have a dual burden as they can be devastating to both public health and animal health, and the most vulnerable people are the millions of poor livestock keepers found globally (Adhikari and Bagale, 2019). These diseases were found further neglected due to the fact that their effect is usually concentrated in developing countries, where the majority of effort in recent years has focused on HIV/AIDs, tuberculosis, and malaria.

Zoonotic diseases listed by WHO are anthrax, avian and other zoonotic influenza, Botulism, Brucellosis, Campylobacter, Chagas disease, Chikungunya, Dengue, E. coli, Echinococcosis, Encephalitis, Foodborne trematode infections, Japanese encephalitis, Leishmaniasis, Leptospirosis, Middle East respiratory syndrome coronavirus (MERS-CoV), Plague, Rabies, Salmonella (nontyphoidal), Severe Acute Respiratory Syndrome (SARS), Spongiform encephalopathies, Streptococcussuis, Taeniasis/cysticercosis, Variant Creutzfeldt-Jakob disease, Zika virus, Zoonotic Tuberculosis and different Haemorrhagic fevers like Crimean-Congo haemorrhagic fever (CCHF), Dengue/dengue haemorrhagic fever, Ebola virus disease, Lassa fever, Marburg virus disease, Rift Valley fever(WHO, 2017).

Zoonoses like Taeniasis/cysticercosis/Neurocysticercosis, Leptospirosis, Hydatidosis, Brucellosis, Toxoplasmosis, Rabies, Dengue fever and Avian Influenzaare found to have epidemic potential and have been identified as Priorities Zoonotic Diseases in Nepal (Adhikari & Bagale, 2019; Ministry of Health and Population, 2011). More than 35000 people take post-exposure treatment in rabid animal bite per annum, and about 100 people die annually due to rabies. Number of case of dog and snake bites is increasing in the country but there is a decreasing trend of death (Ministry of Health and Poulation, 2020). Nepal is a country with diverse ethnic, linguistic and socio-economic characteristics where most of the farmers cultivate mixed crops and rear livestock according to their family needs. They follow traditional practices of rearing which may increase risk for zoonoses. Although people are shifting to commercial farming due to the globalization, industrialization and commercialization; different social problems like illiteracy, poverty, traditional practices might have strong association with zoonotic diseases prevalence in countries like Nepal (Adhikari and Bagale, 2019). In this review we discuss about the current scenario of prioritised zoonotic diseases of Nepal along with role of veterinarian to control zoonotic diseases.

A. Viral Disease

1. Rabies

Rabies is a fatal, but vaccine preventable viral zoonotic disease of mammals caused by Lyssavirus of Rhabdoviridae family (Finnegan *et al.*, 2002). Rabies has been known since around 2000 BC and first written record of rabies is in the Mesopotamian Codex of Eshnunna (Circa 1930 BC) (Adamson, 1977). The virus is present in saliva and brain of infected animals with incubation period of 30 days to 90 days in average (Knobel *et al.*, 2005). The disease is transmitted mainly by the saliva from the infected animals, and 99% of the human rabies cases are through biting and scratching of rabid dog in Asian countries and transmission by bats and other animals poses a significant threat in America, Africa, and Eurasia (Knobel *et al.*, 2005).Rabies virus also gets transmitted if the mucosa and open wound comes in contact with saliva of the affected animals (Hankins and Rosekrans, 2004). Encephalitic form of rabies which accounts for 80% of cases is characterized by symptoms like hyper excitability, autonomic dysfunction, hydrophobia, and aerophobia and the paralytic form is characterized by symptoms like flaccid paralysis in the bitten limb, which ascends symmetrically or asymmetrically. Once these symptoms develop in patient, the disease is invariably fatal (Leung *et al.*, 2007).

Rabies has been reported in more than 150 countries and territories, and dogs contribute up to 99% of all rabies transmissions to humans which are the main source of human rabies deaths (Knobel *et al.*, 2005). Rabies causes tens of thousands of deaths every year, mainly in Asia and Africa where 40% of people bitten by suspected rabid animals are children under 15 years of age from developing countries. In human incubation period of rabies is about 20 to 60 days in average until first symptoms occur (Finnegan *et al*., 2002). First unspecific prodromal stage lasts for about 2 to 10 days until the onset of acute neurological phase, which includes paralysis, spasms of the throat, delirium, hallucinations, coma, cardiac arrhythmia, and finally death. It takes about 30 to 90 days from exposure to death in average but it may take as little as few days or as long as many years(Haupt, 1999). Controlling rabies in dogs can significantly reduce human exposure. So, vaccinating domestic dogs against rabies is an effective means of controlling rabies in dogs by disrupting the transmission of virus among dogs (Ghosh *et al.*, 2020). WHO leads the collective "United against Rabies" to drive progress towards "Zero human deaths from dog-mediated rabies by 2030" (Durrheim and Blumberg, 2017).

Acute encephalitis is caused by rabies virus in all warm-blooded hosts which always has almost fatal outbreak. The first symptoms of rabies may be nonspecific including lethargy, fever, vomiting, and anorexia. Specific signs can be seen within days like cerebral dysfunction, cranial nerve dysfunction, ataxia, weakness, paralysis, seizures, difficulty breathing, difficulty swallowing, excessive salivation, abnormal behaviour, aggression, and/or self-mutilation (Tarantola, 2017).Wound washing with soap water immediately after contact with a suspected rabid animal is crucial and can save lives(Nigg and Walker, 2009).Engagement of multiple sectors and One Health collaboration including community education, awareness programs and vaccination campaigns can reduce rabies patient. Vaccination of dogs, ferrets, and livestock can be after three months of age and a booster vaccination should be administered one year after initial vaccination (Tarantola, 2017).

In every ten minutes, someone in the world dies from rabies, and every year rabies nearly kills about 70,000 human lives annually in over 150 countries with 95% of cases occurring in Africa and Asia (Yousaf *et al.*, 2012). With an estimated 35,172 human deaths per year, rabies is a major burden in Asia, and India accounts for 59.9% of rabies deaths in Asia and 35% of deaths globally. In Africa, about 21,476 human deaths occur each year due to dog-mediated rabies(Hampson *et al.*, 2015). Every year, around 20,000 to 40,000 animal bites were reported in the last five years (2014-2018) in Nepal. 39,744, the highest number of animal bites was reported in year 2016/17 while 20,610, the lowest number of animal bites was reported in year 2014/15. Among total bites, dogs were responsible for more than 90% of bites each year (Pantha *et al.*, 2020). In Nepal, about 100 livestock and 10-100 human are recorded to be dead because of rabies each year along with 1000 livestock and 35000 humans are recorded to have post exposure treatment. 96% of human cases of rabies in Nepal is recorded due to stray and community dogs (Devleesschauwer *et al.*, 2016). 230 cases in year 2017 and 159 cases in year 2018 of rabies were reported in animals (Pantha *et al.*, 2020). Various activities are carried across Nepal for the control of the rabies. Prophylaxis ARV is produced in Nepal at Rabies Vaccine Production Laboratory, and the insufficient demand of ARV is fulfilled by importing vaccine from other countries mainly India. Various animal welfare organizations such as Animal Nepal, Kathmandu Animal Treatment (KAT) center, Sneha's Care, Himalayan Animal Rescue Trust (HART) etc. and various Kennel Clubs are working in the management of stray dogs population and rabies control activities in Nepal (Devleesschauwer *et al*., 2016). For the control and prevention of rabies in Nepal there is only way of one health approach in which stakeholders related to dog, human and rabies need to work together (Acharya *et al.*, 2021).

Coordinated data sharing, risk analysis and effective surveillance, laboratory strengthen, increase in vaccination coverage, advocacy and awareness campaign and proper management of municipal waste can help in containment of rabies in Nepal (Acharya *et al*., 2020; Wright *et al*., 2021; Mahato *et al*., 2020).

2. Avian Influenza

Avian influenza is a highly pathogenic zoonotic disease of avian species caused by Influenza Type A virus of Orthomyxoviridae family (Pham *et al*., 2006). Influenza type A virus is divided into different subtypes based on two proteins, hemagglutinin (H) and neuraminidase (N), present on the surface of the virus. There are 18 different hemagglutinin subtypes (H1 to H18) and 11 different neuraminidase subtypes (N1 to N11), and there are potentially 198 different influenza A subtype combinations, but only 131 subtypes have been detected in nature (Alexander, 2007). The first case of avian influenza was recorded in 1996 in China, and the first human case was reported in 1997 at Hong Kong (Chan, 2002).Avian influenza virus strains are classified into two categories i.e., low pathogenic avian influenza (LPAI) and highly pathogenic avian influenza (HPAI). HPAI infection is clinically important and causes high mortality among the avian species (Pham *et al.*, 2006).Avian influenza virus gets transmitted from bird to bird through direct contact, among one farm to other farm through movement of domestic birds, equipment's, vehicles and even the movement of people (Ungchusak *et al.*, 2005).

Avian influenza type A viruses generally do not infect human population, but rare cases of human infection with these viruses have been reported. People who are in close contact with infected birds are at risk for acquiring avian influenza. Avian influenza virus are found in saliva, mucous and feces of infected birds, and human infections can happen when enough virus gets into a person's eyes, nose or mouth, or is inhaled(Beigel *et al.*, 2005). Through a process of genetic re-assortment, mutation or both, an outbreak of avian influenza in poultry could introduce new avian influenza subtypes into human population, and if a novel AIV emerged with the ability of human-to-human transmission then there is a potential of AIVs leading to devastating human population losses (Beigel *et al.*, 2005; HUI, 2008). Avian influenza type A virus infections in humans shows different signs and symptoms ranged from mild to severe and includes conjunctivitis, influenza like illness (e.g. fever, cough, sore throat, muscle aches) sometimes accompanied by nausea, abdominal pain, diarrhea, vomiting, severe respiratory illness (e.g., shortness of breath, difficulty breathing, pneumonia, acute respiratory distress, viral pneumonia, respiratory failure), neurologic changes (altered mental status, seizures), and the involvement of other organ systems. Including the most serious illnesses and the highest mortality, Asian lineage H7N9 and HPAI Asian lineage H5N1 viruses have been responsible for the most human illness worldwide to date (Apisarnthanarak *et al.*, 2004).

Avian influenza affects both domestic and wild birds, but AI viruses have also been isolated from mammalian species including rats, mice, weasels, ferrets, pigs, cats, tigers, dogs and horse in low frequency (Garamszegi and Møller, 2007). Influenza is most diversified in birds, particularly in wild waterfowl (Tweed *et al.*, 2004).Wild birds are natural host and reservoir for all types of avian influenza viruses which play a major role in the evolution, maintenance, and spread of AI viruses (Spackman, 2008). Avian influenza A viruses have been isolated from more than 100 different species of wild birds and most of them are LPAI viruses. Infection of poultry with LPAI viruses may cause no disease or mild illness (such as ruffled feathers and a drop in egg production), and may not be detected but infection with HPAI can affects multiple internal organs with mortality up to 90% to 100%, often within 48 hours (Huai *et al.*, 2008).

Human infections with the HPAI H5N1 virus were first reported in 1997 during an outbreak in poultry in Hong Kong SAR, China. Since 2003, this avian virus has spread from Asia to Europe and Africa, and has become endemic in poultry populations in many countries. The outbreak causes infection in millions of poultry population, several human cases and many human deaths (Chatziprodromidou *et al.*, 2018). Globally, there are total 861 confirmed human cases of avian influenza A(H5N1), and among them 455 death cases has been reported till date(Subedi *et al.*, 2020). The outbreaks of AIV in poultry have seriously impacted livelihoods, the economy and international trade in affected countries (Sengupta *et al.*, 2007). Regarding Nepal, the first case of avian influenza was recorded in 2009 at the eastern part of the country and, the first human case was recorded in 2019 which resulted in death (Acharya *et al.*, 2020; Subedi and Kaphle, 2019). Since, the first outbreak in 2009 to the fiscal year 2016/2017, total number of 237 HPAI outbreak is recorded in Nepal and 1,966,745 birds are slaughtered (Acharya *et al.*, 2020). After the incidence of first human case of avian influenza in Nepal, awareness among the people, especially the poultry workers, veterinarian, businessman is increasing regarding the maintenance of proper safety measures while working at the farm. Proper biosecurity measures, quarantine, movement restriction of suspected birds, proper disposal of the suspected carcass and litter are to be done, also proper surveillance of the infection is to be done and in the case of the infection, the birds are to be slaughtered and disposed properly (Subedi *et al*., 2020).

3. Japanese Encephalitis

Japanese encephalitis is a vector borne viral zoonotic disease affecting human, pigs and water birds caused by single stranded positive sense RNA flavivirus/Japanese Encephalitis virus, and the risk of the disease is present mainly in countries of south east Asia and west pacific region(Solomon *et al.*, 2000). Japanese encephalitis develops in patients after an incubation period of 5–15 days (Ghosh and Basu, 2009). JE virus is transmitted through a zoonotic cycle between mosquitoes, pigs and water, whereas humans are accidentally infected, and are a dead end host because of low level and transient viremia (Misra and Kalita, 2010). The disease is transmitted to human through the bite of culex mosquitoes. Water birds are the source of virus i.e., the natural maintenance host, but pigs act as the major amplifier host after being infected by the mosquitos, but in case of human, they act as a dead-end host as well as other animals like horse, cattle, sheep, goat, dog, cats, wild mammals etc. are also affected sub-clinically by the virus (Misra and Kalita, 2010; Solomon *et al.*, 2000).

Japanese encephalitis is one of the most important endemic encephalitis in the world especially in Eastern and South Eastern Asia, and scientific evidence predicts that it will become a global pathogen and cause of worldwide pandemics soon (Ghosh and Basu, 2009; Misra and Kalita, 2010). Long-term travellers, persons involved in outdoor activities or on work assignments going to endemic areas are at risk, especially those visiting rural areas, farms, rice fields and irrigation areas and children under 15 years of age seem to be particularly susceptible to the infection(IAMAT, 2020). This JE virus is a neurotropic flavivirus that affects the central nervous system which causes extensive damage that may lead to fatality rate as high as 30% among those with disease symptoms and half of the survivors will suffer from severe neuropsychiatric sequelae (Dutta *et al.*, 2010).Gastrointestinal pain and vomiting may be the dominant initial symptoms in children and severity of disease is characterized by rapid onset of high fever, headache, neck stiffness, disorientation, coma, seizures, spastic paralysis and ultimately death (Michael and Solomon, 2012). Japanese encephalitis infection can be prevented by using insect repellent, wearing long-sleeved shirts and long pant and by vaccination (Fischer *et al.*, 2014).

Horses are the primary affected domestic animals of Japanese encephalitis, but other equids like donkeys are also susceptible. Pigs act as important amplifiers of the virus producing high viremia that infect mosquito vectors, and birds of the family Ardeidae are natural maintenance reservoir for JE virus (Ellis *et al.*, 2000). Horse shows three main clinical syndromes; transient, lethargic and hyperexcitable. High fever up to 40 °C, anorexia, and sluggish movement congested or jaundiced mucous membranes are seen in the transient type syndrome, and recovery was uneventful. Fever fluctuating from 38.8°C to 41°C occurred in association with lethargy, anorexia, nasal discharge, difficulty in swallowing, jaundice, and petechial hemorrh age on mucous membranes, incoordination, staggering, and falling etc. are seen in lethargic type and horses usually recovered in 4 to 5 days. High fever (> 41°C), aimless wandering about, sudden shying at imaginary objects, violent behavior, and blindness, profuse sweating, teeth grinding, and spasmodic muscle twitching are seen in hyperexcitable type, which occurred in less than 5% of clinical cases. In some cases of hyperexcitable type, the severe signs disappeared after 8 hours, but collapse and death of severely affected horses in 24 to 48 hours was common (Ellis *et al.*, 2000). JE is commonly seen as a reproductive disease in pigs and reproductive losses can be reached up to 50–70%. Abortions in sows, stillbirths or mummified fetuses, reduced number and motility of sperm in boars are the common clinical findings of JE in pigs. Live born piglets most often shows neurological signs of tremors and convulsions and may die soon after birth (Mansfield *et al.*, 2017).

The first case of Japanese Encephalitis was identified in 1871 in Japan (Erlanger *et al.*, 2009). JE virus is the main cause of viral encephalitis in many countries of Asia with an estimated 68,000 clinical cases, and around 13,600 to 20,400 people die of this disease every year. More than 20countries in South-East Asia and Western Pacific regions have JEV transmission risk exposing more than 3 billion people to risks of infection (Quan *et al.*, 2020).The very first case of this disease in Nepal was identified in 1978. 1,823 human cases of Japanese encephalitis was found in Nepal from 2007-2015 which suggests that it is a reoccurring zoonotic disease which exists in the endemic form (Pant *et al.*, 2017).

B. Bacterial Diseases

1. Leptospirosis

Leptospirosis is the most widespread zoonosis worldwide. It infects human and different species of animals which is caused by different serovar of *Leptospira* (Bharti *et al.*, 2003). It is a systemic disease of humans and domestic animals mainly dogs, cattle and swine, characterized by fever, renal and hepatic insufficiency, pulmonary manifestations and reproductive failure (Adler and de la Peña Moctezuma, 2010). Clinical signs are quite variable, and different animals are the reservoir of different serovar of Leptospira such as *Canicola* in dogs, *Bratislava* in horses and pigs, *Hardjo* in cattle and *Australis* and *Pomona* in pigs (Levett, 2001). The bacteria gets transmitted through the contact with the urine of the infected animal, and the urine contaminated environment of the infected animals; the bacteria enters the animal/human body through the skin abrasion, mucus membrane and also through the water and feed contaminated with urine and other body secretions (except saliva) of infected animals (Wynwood *et al.*, 2014).

Human gets infected with leptospirosis through the contact with urine and other body fluids except saliva from infected animals or contact with water, soil, or food contaminated with the urine of infected animals(Maze *et al.*, 2018).Many wild and domestic animals can serve as reservoir hosts for this disease, but the brown rat (*Rattusnorvegicus*) is the most important source for human infections. Individuals living in urban slum environments with inadequate sanitation and poor housing are at high risk of rat exposure (Haake and Levett, 2015). Leptospirosis can cause a wide range of symptoms in human including high fever, headache, chills, muscle aches, vomiting, jaundice (yellow skin and eyes), red eyes, abdominal pain, diarrhoea and rashes on skin. Many of these symptoms can resemble with other diseases, and in some cases infected persons may have no symptoms at all (Haake and Levett, 2015).The time between a person's exposure to a contaminated source and becoming sick is 2 days to 4 weeks and mortality increases with age, particularly in patients older than 60 years of age(Haake and Levett, 2015).

In dogs, typical leptospirosis may present with fever, jaundice, vomiting, diarrhoea, and intravascular disseminated coagulation, uraemia caused by renal failure, haemorrhages and death (Bolin, 1996). Signs of infected cattle and pigs include reproductive failure, abortion, stillbirths, fetal mummification, weak piglets or calves and agalactia. In horses, a chronic manifestation of leptospirosis is commonly seen as recurrent uveitis(Rohrbach *et al.*, 2005). Recovering animalsmay become asymptomatic carriers carrying virulent leptospires in the renal tubules for extended periods and shedding infectious leptospires into the environment (Adler & de la Peña Moctezuma, 2010). Other species such as mice and rats serve as reservoirs for their host-related serovars (mice for Ballum, Icterohaemorrhagiae and rats for Copenhageni) (Bharti *et al.*, 2003).

Annually, about 1,03,000 cases of Human Leptospirosis is reported, and about 58,900 death are recorded every year globally (Costa *et al.*, 2015).A serological analysis of 144 patients of terai region of Nepal showed that 30 patient i.e. 21% of the patient were positive to *Leptospira*s pecies (Regmi *et al.*, 2017). Also the analysis of 993 patient with acute encephalitis negative for Japanese Encephalitis from 2007-2008 resulted in 416 i.e. 41.8% positive case of Leptospirosis (Bhattachan B, 2017), and a similar analysis of 778 patients serum at National Public Health Laboratory in 2008 resulted in 402 i.e. 51.7% positive leptospirosis cases(Board, 2013). Among the 70 dog's blood sample collected from Kathmandu at 2016, on serological analysis 9 sample i.e. 11.4% was positive for Leptospira (KC *et al.*, 2018). In serological analysis of 200 infertile animals (114 cows and 86 buffaloes), 8.5% animals (11% cows and 5.5% buffaloes) were positive for *Leptospirahardo* (Joshi, 2000).

2. Salmonellosis

Salmonella are the gram-negative zoonotic bacteria of Enterobacteriaceae family and has more than 2500 serotypes. Salmonellae are a diverse group of organisms; the differentiation of the organisms being based on biochemical and serological characteristics (Murray, 1991). Salmonella are food borne bacteria and the causes of 1 out of 4 diarrheal disease and some infections in human (Endt *et al.*, 2010). They often cause subclinical infections and may shed in large numbers within the faeces which result contamination of the environment. Infection in food animals often leads to contamination of meat, eggs, milk and cheese. Salmonellosis is one of the most common and economically important food-borne zoonotic diseases in humans which have been recognized in all countries, and non-typhoid salmonella appears to be most prevalent in areas of intensive animal husbandry, especially in pigs, intensively reared calves and poultry(Coburn *et al.*, 2007).Salmonella is major infectious bacteria of avian species, mainly *S. pullorum* and *S. gallinarum*. It infects avian species and causes pullorum and typhoid (Gast and Porter, 2020). Consumption of these contaminated poultry meat raw or improperly cooked causes gastroenteritis in human (Vandeplas *et al.*, 2010).

Salmonella causes typhoid to human, and also causes gastroenteritis leading to diarrhoea, fever and stomach cramps in human (Padungtod and Kaneene, 2006). People may also have nausea, vomiting, or a headache and symptoms usually start within 6 hours–6 days after infection and last 4–7 days (Brent *et al*., 2006). Salmonellosis in humans is generally contracted through the consumption of contaminated food of animal origin like eggs, meat and milk, although other foods including green vegetables contaminated by manure also play role in its transmission. Person to person transmission can also occur through the faecal oral route, and direct contact with infected animals including pets may also cause infection (Tondo and Ritter, 2012). Animals become infected with Salmonella through their environment, by eating contaminated food or from their mothers before they are born or hatched. All species of animals including poultry and wild birds, farm animals (goats, cows, sheep, and pigs), horses, dogs, cats and others animals like reptiles, rodents and amphibians got infected by this disease, but young and pregnant are more susceptible (Coburn *et al.*, 2007). Many clinical signs are shown by affected animals including acute septicaemia, acute or chronic diarrhoea, respiratory disease, abortion, and arthritis. Chicks and poultry of less than 1 week of age are highly susceptible to Salmonella infection and different signs including anorexia, adipsia, depression, ruffled feathers, huddling together, somnolence, dehydration, white diarrhoea and pasted vents with considerable mortality may be reported *(Gharieb et al.*, 2015).

Salmonella infections are responsible for a significant burden of morbidity and mortality worldwide. There are about 11–21 million cases of typhoid fever and approximately 128,000–161,000 deaths. The majority of cases are found in South and South-East Asia and sub-Saharan Africa (WHO, 2018). Non typhoidal salmonellae are one of the leading causes of bacterial diarrhoea worldwide; they are estimated to cause approximately 153 million cases of gastroenteritis and 57,000 deaths globally each year (Stanaway *et al.*, 2019). Fowl typhoid and pullorum disease are mainly distributed in Latin America, the Middle East, Africa and perhaps in the other parts of the world and have economic significance (Geetha and Palanivel, 2018). Salmonellosis is one of the leading diseases of fever in most of the hospitals in Nepal. As shown by annual report published by Department of Health Service (DoHS) of Nepal, the prevalence of typhoid fever is very high in different mountains, valleys and southern belts of Nepal from May to August (ENPHO, 2020). Out of 123 raw meat samples (55Chickens, 37 Buffaloes and 31 Goat) from Kathmandu Metropolitan City, 11.4% i.e. 14 sample were tested positive for salmonella (8 Chicken, 5 Buffaloes and 1 Goat)(Vandeplas *et al.*, 2010). The increasing antibiotic resistant *Salmonella* species further increases the risk to the human consumption. In a study carried at Dharan, a city of Province No.1of Nepal showed that 100% of *Salmonella* positive meat samples was resistant to amoxicillin, 24% to tetracycline, 11% to nalidixic acid and 11% to chloramphenicol (Bantawa *et al.*, 2019). Proper hygienic practices at animal farm, during transportation of animals, managed and hygienic slaughtering method, processing units, storage and transportation helps to reduce the bacterial load in meat, also proper cooking of the meat before consumption also decreases health risk of people (Herman *et al.*, 2003; Vandeplas *et al.*, 2010).

3. Brucellosis

Brucellosis is a zoonotic bacterial diseasealso known as undulant fever, Malta fever, and Mediterranean fever(Pierdomenico *et al.*, 2011) caused by different species of Brucella which affects different species of animal like cattle, buffaloes, sheep, goat, horse, dog, pig etc., and the disease is transmitted to human through direct and indirect contact with infected animals and their products (Corbel, 2006).Different species of Brucella affect different animals like *B. abortus*affects mainly cattle; *B .melitensis* mainly affects small ruminants like goat and sheep; *B. ovis* mainly affects sheep; *B. swis* mainly affects pig; *B. canis* mainly affects dogs (Poester *et al.*, 2013).Different species of Brucella are recorded in human mainly *B. abortus, B. melitensis, B. canis and B. suis*. Brucellosis has been recognized in animals and humans since the early 20th century (Young, 1983).

Human brucellosis has a major impact on public health, even though successful eradication and control programmes for domestic animals have been established in many countries around the world (Al Dahouk *et al.*, 2013). Brucellosis infection in humans occurs by penetration through damaged skin, conjunctiva, and more rarely via the alimentary route by the consumption of infected products. Especially veterinarians, veterinary technicians, insemination service employees, zoo technicians, farmers, employees of slaughter houses and meat processing enterprises are on risk. Human to human transmission and sexual transmission in human has rarely been reported (Meltzer *et al.*, 2010). Human brucellosis has a broad spectrum of clinical manifestations, which can vary from subclinical infection with fever; osteoarticular involvement; sweating; constitutional symptoms; and hepatic, cardiac, central nervous system, or ocular involvement (Zhang *et al.*, 2010).

In female animals, brucellosis is characterized by abortion, placenta retention, vaginal secretions, low fertility rate and also embryonic and neonatal death. In males, clinical findings include epididymitis, orchitis, uni or bilateral testicular atrophy, sperm abnormalities and infertility. Lymphadenopathy, hepatopathy, splenomegaly, uveitis and discospondylitis may also be observed in dogs. In horses, the typical clinical sign is characterized by a granulomatous supraspinous or supra-atlantal bursa lesion. Infected animals can also be asymptomatic and every infected symptomatic or asymptomatic animals can play an important role on infection to other animals and humans (Megid *et al.*, 2014). The clinical picture is not specific in animals or humans and diagnosis needs to be supported by laboratory tests (WHO, 2006).

Brucellosis is the second most important zoonotic disease in the world after rabies according to the World Organization for Animal Health. 1 to 200 new human cases of brucellosis per 10 million individuals every year have been recorded (Acharya *et al.*, 2016). Around 500,000 cases of human brucellosis are recorded annually around the world (Harrison and Posada, 2018).The highest incidence is observed in the Middle East, the Mediterranean region, sub-Saharan Africa, China, India, Peru, and Mexico. Currently, countries in central and southwest Asia are observing the greatest increase in cases. Several countries in Western and Northern Europe, Canada, Japan, Australia and New Zealand are believed to be free from the agent(Pappas *et al.*, 2006). The first human case of brucellosis in Nepal was recorded in 1979 from Kaski district (Acharya, 2016). Brucellosis has been reported to be endemic in Nepal, but neither the distribution nor the economic and public health impact of the disease is well characterized (Jackson *et al.*, 2014). In a study carried out by Joshi reported a prevalence of 6.08% in humans, 8.70% in cattle, and 3.64% in sheep and goats (Acharya, 2015). In a serological analysis of different species of animals at Kailali district of Nepal 12% i.e. 28 out of 233 were positive for brucellosis; 325 cattle i.e. 16 out of 50, 13.4% buffaloes and 2.6% goat i.e. 3 out of 113 were positive (Pandeya *et al.*, 2013). Based on the nationwide surveys, Department of Health Service reported that approximately 2% to 3% of cattle in Nepal are sero-positive for brucellosis (Acharya *et al.*, 2016).

C. Protozoan Diseases

1. Cysticercosis

Cysticercosis is an infection by the larval cyst of *Taenia solium* in brain, muscle and other tissues and causes epilepsy and seizure in human population(Garcia and Del Brutto, 2000).The larval stage of the *Taenia solium* infects the human nervous system which causes neurocysticercosis, a disease which is one of the main causes of epileptic seizures in many less developed countries and is also increasingly seen in more developed countries because of immigration from endemic areas (García *et al.*, 2003). *Taenia solium* naturally affects the pigs. When raw or improperly cooked meat are ingested by human then the human gets the worm which grows in the intestine of human and release as eggs bearing gravid proglottids. Faeco-oral ingestion of these gravid proglottids leads to the development of the cysticercosis in human which may be neuro-cysticercosis (NCC), visceral, muscle or subcutaneous cysticercosis (Gonzales *et al.*, 2016).

Human cysticercosis, infection with the larval stage of the pork tapeworm, is a modern human plague which affects thousands of people world-widely(Del Brutto and Del Brutto, 2013). Cysticerci may invade almost every organ of the human, but it is most often related to invasion of the central nervous system, giving rise to neurocysticercosis. Cysticerci found in extra neural structures including subcutaneous tissues, striated muscles and even the heart, liver or other organs (Del Brutto, 2013). With the exception of massive muscle infection by hundreds of cysticerci causing muscular pseudo-hypertrophy or some sporadic cases of cardiac arrhythmias related to a cardiac cyst, most cases of systemic cysticercosis are clinically irrelevant and their presence just suggest that an individual may also have neurocysticercosis (Sawhney *et al.*, 1976).Cysticercosis doesn’t spread by eating undercooked infected pork, but people get infected with tapeworms (taeniasis), and people who have tapeworm infections can infect themselves with the eggs and develop cysticercosis (autoinfection) (Dermauw *et al.*, 2018; Flisser *et al.*, 1979).

Cysticercosis affects the muscles of infected animals. Cattle and pigs are more commonly affected by this(Flisser *et al.*, 1979). Bovine cysticercosis (also known as bladder worm or beef tape worm) is caused by *Taenia saginata* which causes few symptoms in the animal, but an important zoonosis. However, heavy infections of bovine cysticercosis may cause myocarditis and heart failure associated with developing cysts in the heart (Scandrett *et al.*, 2009). The tapeworm larvae live in the animal's muscle tissue, particularly the heart, facial muscles surrounding the jaw, diaphragm and tongue. Bovine cysticercosis is therefore difficult to diagnose in live animals, but if the animal is heavily infested, cysts may be felt on the tongue and face (Blagojevic *et al.*, 2017).

Confirmation of same causative agent for taeniasis and cysticercosis was provided during the 19th Century (Del Brutto and García, 2015). Neurocysticercosis causes 50,000 deaths/year, and is the most common cause of acquired epilepsy worldwide, around 30% of epilepsy seen in the developing world is due to neurocysticercosis (Del Brutto, 2013). It is estimated that three quarters of the estimated 50 million people with active epilepsy live in the poor countries of the world (Prasad *et al.*, 2008).In many endemic areas where human and pigs live in close proximity 30% of the epilepsy is due to NCC, and in high risk areas it may be up to 70%(Dermauw *et al.*, 2018). In a study at Manipal Teaching Hospital Pokhara, out of 1355 cases of seizure from2003-2015 among the age group of 0-17years, 16.90% i.e. 229 were positive for NCC which showed the high rate of prevalence of cysticercosis in Nepal (Rao *et al.*, 2017). Regarding the case in pigs, out of 110 slaughtered pigs for the study at the Banke district of Nepal 295% i.e. 32 were positive for *Taeniasolium*, and 27% i.e. 30 had the viable cysticerci (Sah *et al.*, 2017). Close proximity of pig and human, and also the practice of consuming raw or improperly cooked meat of pig have increased the cases of cysticercosis in Nepal.

2. Hydatidosis

Hydatidosis also known as cystic echinococciosis is a parasitic zoonotic disease caused by tapeworm *Echinococcus granulosus*, adult of which are harbored in the intestine of dog, foxes and other carnivorous; the eggs of the parasite are released in their feces and the human infection occurs by the ingestion of these egg which develops to larvae and reaches to different organs especially liver and lungs (Matossian *et al.*, 1977). Intermediate host of this tapeworm are cattle, sheep, goat and pig (Macpherson, 1985).

Persons with hydatidosis often remain asymptomatic until hydatid cysts containing the larval parasites grow large enough to cause discomfort, pain, nausea, and vomiting. Although most infections in humans are asymptomatic, hydatidosis causes harmful, slowly enlarging cysts in the liver, lungs, and other organs that often grow unnoticed and neglected for years (Grosso *et al.*, 2012).The cysts are mainly found in the liver and lungs but can also appear in the spleen, kidneys, heart, bone, and central nervous system, including the brain and eyes. Cyst rupture is most frequently caused by trauma and may cause mild to severe anaphylactic reactions, even death, as a result of the release of cystic fluid(Gottstein and Reichen, 2002).

Like all tapeworms the life cycle of hydatidosis involves two animals. A carnivore is the definitive host where the adult worms live in the intestines and almost any mammal, including humans can be the intermediate host where the worms form cysts in various organs(Macpherson, 1985).In livestock there can be reduced growth, decreased production of milk, meat and wool. However, the cysts grow slowly so that many infected animals are slaughtered before the cysts ever cause disease problems.There may be multiple cysts in the brain, kidneys, bones, or testes causing more severe illness. Without control measures, infection rates can be very high in livestock and dogs, with associated significant incidence in humans(Armiñanzas *et al.*, 2015).

Hydatidosisis globally distributed and found in every continent except Antarctica. In endemic regions, human incidence rates for hydatidosiscan reach more than 50 per 100 000 person-years, and prevalence levels as high as 5%–10% may occur in parts of Argentina, Peru, East Africa, Central Asia and China. In livestock, the prevalence of hydatidosisfound in slaughterhouses in hyperendemic areas of South America varies from 20%–95% of slaughtered animals(Toulah *et al.*, 2017).The highest prevalence is found in rural areas where older animals are slaughtered. Depending on the infected species involved, livestock production losses attributable to cystic echinococcosis results from liver condemnation and may also involve reduction in carcass weight, decrease in hide value, decrease of milk production, and reduced fertility(WHO, 2020).This disease has created public health and environment problems in all urban areas of Nepal(Joshi *et al.*, 1997).In the Banke district out of 68 slaughtered pigs 36% i.e 25 were found to have cystic echinococciosis(Donadeu *et al.*, 2020).According to paper by Joshi, the highest prevalence of *E. granulosus*(5/88=5.7%) was seen in domestic dogs from an areaof Kathmandu city. The carcasses of the animals wereexamined and hydatid cysts were found in waterbuffalo 5% (153/3,065), goat 3% (55/1,783), sheep 8% (12/150) and pig 7% (10/143) in 17 differentabattoirs in Kathmandu(Joshi et al., 1997).

3. Toxoplasmosis

Toxoplasmosis is a zoonotic parasitic disease caused by intracellular protozoan parasite *Toxoplasma gondii.* The natural definitive host of which is domesticated cats and members of family Felidae and the intermediate host of the parasite are birds and rodents but other mammals including humans are also affected (Hill and Dubey, 2002). Human infection of the parasite occurs by consumption of uncooked meat of animal harbouring tissue cysts, by consumption of food and water contaminated with cat feces containing un-sporulated oocyst also by blood transfusion or tissue transplantation and trans placentally from mother to fetus (Saadatnia and Golkar, 2012). Toxoplasmosis is particularly more serious in pregnant women as the disease may result in stillbirth, miscarriage and child disability (Kravetz and Federman, 2005).

Toxoplasmosis may cause flu-like symptoms in some people, but most people affected never develop signs and symptoms. For infants born to infected mothers and for people with weakened immune systems, toxoplasmosis may cause serious complications (Esch, 2010; Pal *et al.*, 2014). Symptoms shown by toxoplasmosis similar to flu include; body aches, swollen lymph nodes, headache, fever and fatigue (Esch, 2010; Hill and Dubey, 2002). People with weak immune system shows more-severe signs and symptoms of infection like severe headache, confusion, poor coordination, seizures, lung problems and blurred vision caused by severe inflammation of retina (ocular toxoplasmosis)(De Jong, 1989).

Toxoplasmosis infects wild and domestic animals including birds, cats, sheep, goats, cattle, pigs and poultry. Cats are the most common source of the Toxoplasma protozoa that are transmitted to other animals or people (Innes, 1997).Toxoplasmosis causes general clinical signs, such as fever, anorexia, or dyspnea, and more specific signs with neural, respiratory, cutaneous, or ocular involvement. Because of the wide range of clinical signs, the diagnosis in domestic and pet animals can be complicated (Calero-Berna and Gennari, 2019).

Toxoplasmosis is prevalent in every country, and seropositivity rates range from less than 10% to over 90% (Torgerson and Mastroiacovo, 2013). Toxoplasmosis is becoming a global health hazard as it infects 30-50% of the world human population (Flegr *et al.*, 2014). More than 40 million men, women, and children in the U.S. carry the Toxoplasma parasite, but very few have symptoms because the immune system usually keeps the parasite from causing illness (CDC, 2019). Reportedly, nearly half of the Nepalese are Toxoplasma seropositive but the first case of congenital toxoplasmosis was reported on 2011 in a 53 days old male baby. On a serological analysis of 336 blood sample of different species including human at Sunsari district 12.67% human i.e. 19 out of 150, 12% sheep i.e. 6 out of 50, 8.7% cattle i.e. 8 out of 92 and 36.36 % i.e. 16 out of 44 were positive for toxoplasmosis. Also, the same study showed that the occurrence of human toxoplasmosis was more among the farmers followed by butcher, and most of the positive human had contact with cats (Sah *et al.*, 2018).

Role of Veterinarian to Fight Against Zoonotic Diseases

Veterinarian as Crucial Part of One Health

Veterinarians are at frontline of one health approach which takes human, animal and environment as a single unit. The major objective of one health approach is to control the zoonotic diseases and protect all these components. As these diseases are transmitted among animals and human, both the human doctor and veterinarian have a great role to play for the control of the diseases and its spread. Proper surveillance of disease among different species of animals, diagnosis of these diseases, and proper treatment and control of spread of these diseases are the responsibilities of veterinarians. Proper analysis of the edible animal products i.e., milk, meat and egg before consumption, and also proper examination of non-edible products such as wool, fur, hides, bones etc. is essential so as to control the transmission of the diseases from animals to human. Veterinarians are fighting against complex problems like antimicrobial resistance, food security, zoonotic diseases, climate change and wildlife trafficking which all need one health approach for the solution.

Fight Against COVID-19 Pandemic

The outbreak of coronavirus disease 2019 in December 2019 in Wuhan, China and subsequently first outbreak was reported in Nepal on 13 January 2020 (Gautam *et al.*, 2020). In Nepal veterinarians and their laboratories had played significant role in test and diagnosis of the disease. Five animal laboratories were converted for the PCR examination of coronavirus. National Avian Disease Investigation Laboratory, Chitwan/ Bharatpur Hospital COVID-19 Diagnostic Laboratory Regional Animal Disease Investigation Laboratory, Biratnagar/ Provincial Public Health Laboratory Regional Animal Disease Investigation Laboratory, Surkhet/ Surkhet Provincial Hospital Regional Animal Disease Investigation Laboratory, Dhangadi/ Seti Provincial Hospital Regional Animal Disease Investigation Laboratory, Janakpur/ Provincial Public Health Laboratory are still in operation for the diagnostic test of COVID-19. Not only are these veterinarians also involved in surveys and education to fight against this pandemic (Subedi *et al.*, 2020). This pandemic had taught a lesion for one health approach does not have exception for the control of zoonotic diseases in both humans and animals (Poudel *et al.*, 2020).

Treatment of Animal Disease Which Support Public Health and Economy

Outbreak of different animal diseases which may be zoonotic or other are massively affecting not only animal health but also economy and public health. Outbreaks of avian influenza, anthrax, leptospirosis, and cases of rabies, taeniasis are interlinked among human and animals. Veterinarians in Nepal are fighting against such diseases in animal level to protect public health. Other diseases like Foot and Mouth Disease (Kandel *et al.*, 2020), Lumpy Skin Disease (Acharya *et al.*, 2020), PPR causes huge economic loss of farmers so various strategies such as prevalence study, vaccination program, awareness campaign, animal health camps are conducted by veterinarians on regular basis.

Conclusion

These zoonotic diseases reported in Nepal some have proper recording and surveillance while others aren't properly diagnosed and recorded. Lack of proper governmental policy regarding the diagnosis and surveillance of the different diseases is major reason of lack of proper data. Communication gap between stakeholders of animal and human health is the major concern for the control of zoonotic diseases in Nepal. Collaboration, coordination and communication among stake holders of animal health, human health, environmental science and agriculture is urgently needed under the umbrella of One Health for the control and prevention of zoonotic diseases in Nepal.

Authors' Contribution

A Gautam perceived the idea, all authors wrote, reviewed, and approved the final manuscript.

Conflict of Interest

The authors declare that there is no conflict of interest with present publication.

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