

Review

Current scenario of viral diseases and vaccination strategies of cattle in Turkey

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Abstract

The dairy and meat industry has rapidly developed in the last decade in Turkey and is playing a key role in supplying animal proteins for human consumption. Viral pathogens continue to threaten the dairy and meat industry leading to serious economic losses worldwide, including Turkey. The Turkish cattle industry has been vulnerable to the spread of viral diseases within the country in the continent. Combating animal diseases is crucial for the economy of Turkey. A good cattle health management policy may reduce the direct losses associated with viral diseases and thereby lead to increase in export of animals and animal products. Countries that are unable to combat animal diseases remain excluded from international trade. Control and eradication of cattle diseases require the availability of effective and practical interventions including vaccination and biosecurity measures. This review summarises the currently available information about viral diseases in cattle in Turkey and emphasizes the need for disease monitoring and research, along with implementation of disease control measures to mitigate economic losses to farmers and the country. The information presented here can be of great value in the research, prevention, and control of cattle diseases.

Key words: Virus; viral diseases; cattle; dairy; Turkey.

J Infect Dev Ctries 2022; 16(8):1230-1242. doi:10.3855/jidc.14767

(Received 24 January 2021 – Accepted 09 June 2021)

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Introduction

Livestock is considered to be a central component of the agricultural sector of Turkey and plays a vital role in food supply and the Turkish economy. Progressive dairy and meat industries are an important part of the animal production sector. Globally, consumer demand for healthy, hygienic and safe milk and meat products is increasing due to the growing population of people with high purchasing power. In Turkey, cattle are one of the most important livestock in terms of number (14.4 million heads) and make a substantial contribution to achieving food and nutrition security [1]. Cattle farming in Turkey has made considerable progress in recent years towards becoming a well-organised commercial industry with the help of Cattle Breeders Association of Turkey (CBAT), Union of Dairy, Beef and Food Industrialists of Turkey (SETBIR), Cooperative Unions, Union of Agriculture Chambers (ZOB), Turkish Veterinary Medical Association (VHB), and Milk, Meat and Stud Cattle Breeders Association (TUSEDAD). There are

approximately 1.7 million dairy cattle enterprises in Turkey [2]. This sector provides jobs and livelihood to millions of small holder farmers and poor people in the country and plays a significant role in poverty alleviation. Cattle farming in Turkey is not only producing food for local consumers, but also contributing to trade and export of cattle products to neighbouring countries, thus contributing significantly to the Gross Domestic Product (GDP) of Turkey.

Farming operations have become more intensive in the last three decades and have made beef and dairy farm management more challenging. Cattle farms worldwide, including Turkey, are impacted by numerous pathogens that result in huge economic losses due to infectious diseases every year [3,4]. Infectious diseases have a negative impact on the livestock production system, thus setting off a cascading affect of low production, low income, and subsistent livelihood. The consequences of animal diseases in livestock can be complex and generally extend well beyond the immediate impact on the producers. Infectious diseases

lead to productivity losses in the livestock sector (production losses, cost of treatment and market disturbances), loss of income from activities using animal resources (energy, transportation and tourism), prevention or control costs (production costs of vaccines, and public expenditure) and suboptimal use of production potential (animal species, genetics and livestock practices) [5]. Veterinary-treatment costs, vaccination expenses and death of cattle due to infectious diseases can increase the overall cost of production in cattle farms. Mortality and morbidity of cattle due to viral infections have significant effect on the profitability of cattle farming, leading to reduced meat and/or milk production. The economical losses related to viral infections are not exactly known due to insufficient economic assessment of cattle viral diseases in Turkey. In addition, viral pathogens that infect cattle can also be a threat to public health due to their zoonotic potential [6,7].

The major viral diseases affecting Turkish cattle include foot-and-mouth disease (FMD), lumpy skin disease (LSD), pseudocow pox, bovine respiratory disease complex (BRDC), bovine viral diarrhea (BVD), bovine adenoviral disease (BAD), bovine leukemia (BL), bovine papillomatosis (BPV), epizootic haemorrhagic disease (EHD), bovine rotavirus, bovine coronavirus, bovine norovirus (BNV), bovine influenza and Schmallenberg virus (SBV) infections [3,4,8,9].

The incidence or outbreaks of certain diseases in a specific region of a country only represent the regional cattle population and it can not be considered to be the epidemiological situation for the cattle in the entire country. Disease reporting practices may vary in different parts of the country, and therefore a review of published data cannot provide an accurate evaluation of the epidemiological situation across pathogens or countries. In order to gather information and data regarding cattle viral diseases in Turkish cattle herds, scholarly publication databases (PubMed, Science Direct and Google Scholar) were searched extensively for short reports, review articles and research articles. In addition, the World Organisation for Animal Health (OIE) platform World Animal Health Information System (WAHIS) was also used to obtain viral disease related information. In addition to the above-mentioned databases, the NCBI-Genbank® database was also searched for genome sequences that were deposited from Turkey. Veterinary officers from different regions of Turkey were also requested to provide information about outbreaks of certain diseases at cattle farms in their area. The authors have thoroughly cross checked the credibility and originality of the data included in the

current review. The authors have also tried their best to confirm the authenticity of the data with the help of their colleagues working in different Veterinary Institutes of Turkey. Data available before May 2019 were included and any other published or non published data after that date have not been included in this review article.

To the best of our knowledge, there is no published review article on the current scenario of important viral diseases of cattle in Turkey. The main goal of this review is to summarise the data available on important viral diseases of cattle in Turkey. Moreover, current vaccination practices and vaccine-related issues are also highlighted. The information presented here can be of great value in research, prevention, and control of cattle diseases and can be useful for researchers, veterinarians, farmers, food sector and veterinary establishments.

Major viral diseases in Turkish cattle herds

Foot-and-mouth disease

Foot-and-mouth disease (FMD) is an economically important animal disease worldwide. The disease is caused by the foot-and-mouth disease virus (FMDV) which is a single stranded positive sense RNA virus, belonging to the genus *Aphthovirus* in the *Picornaviridae* family [8,10]. FMD affects extensive areas worldwide and is included in the list of diseases notifiable to OIE (<http://www.oie.int/eng/en.index.htm>). FMDV has high transmissibility and can lead to international trade restrictions. When there is an acute infection, affected animals shed the virus in all the body secretions and excretions such as saliva, nasal and lachrymal fluid, milk, urine, feces, semen, and exhaled air. Contact with infected animals and contaminated fomites and fodder directly or indirectly can transmit the disease; although, majority of the transmission events occur by the movement of the infected animals [10-12].

Turkey is included in the group of countries in which FMD is endemic and outbreaks occur from time to time [12,13]; however, the Thrace district of Marmara region of Turkey which borders the European Union is now declared a FMD free zone [13]. An increasing trend in disease incidences were observed between the years 2006 and 2013 [12]. In Turkey, the average annual number of outbreaks of FMD between the years 2006 and 2013 was 1046 [12-14] and outbreaks have continued in recent years. Thirty percent of the animals in East and South East Anatolia were reported to be FMDV positive [15]. In 2009, the seroprevalance for the FMDV was 8.81% in bovine and

ovine animals in Turkey [16] and increased to 21.9% in 2011 [17]. In addition to the high number of outbreaks, production losses due to the disease are in the tens of millions of Turkish Lira [18]. There is a high prevalence of FMD in the eastern and southeastern parts of the country. It is the most susceptible area due to illegal animal movements and low vaccination rate. Therefore, strict quarantine and mass vaccination strategies are being applied in these areas of Turkey along with other regions.

Vaccinations play a crucial role in the control of the FMD and are widely used throughout the world. FMD in Turkey is usually controlled using biannual or triannual mass vaccination of cattle and culling of FMD affected animals [16,17,19]. The trivalent vaccine used in Turkey covers serotypes O, A and Asia-1. Most farms in Anatolia are small holdings dependent upon communal grazing, and vaccination should be performed before the animals are sent out for spring grazing. In autumn, at the end of the grazing season, the cattle are typically kept indoors during winter. Within Turkey, there is great variation in topography, climate and livestock husbandry practices. This results in differences in the seasonality of livestock births and population age structure. These demographic factors determine the proportion of cattle eligible for routine FMD vaccination (≥ 2 -3 months old), the proportion recently vaccinated and the proportion that have received multiple doses [20]. However, the extent to which FMD can be controlled by vaccination alone without effective biosecurity remains uncertain. In addition, education of farmers and new regulations for controlling the disease are urgently needed. Additional

information about farmers in the cattle sector are provided in Table 1.

Bovine herpes virus infections

Infectious bovine rhinotracheitis (IBR), infectious pustular vulvovaginitis (IPV) and infectious pustular balanoposthitis (IPB) are important respiratory and genital diseases of cattle, caused by bovine herpes virus-1 (BHV-1). BHV-1 belongs to the genus *Varicellovirus* in the subfamily *Alphaherpesvirinae* under the family *Herpesviridae*. BHV-1 is shed along with nasal discharge for 10-14 days after the onset of symptoms during acute respiratory infection and transmission occurs by contact with mucosal droplets from infected cattle. Moreover, contaminated materials including semen could also transmit virus to healthy animals [21].

Studies performed in Turkey indicate that the virus is endemic among dairy and beef cattle populations [22-27]. The disease is notifiable in many countries but not in Turkey. Screening, surveillance, vaccinations, precautions at borders, and eradication policies, are currently being implemented to control BHV-1. The BHV-1 seropositivity rates among cattle were between 9.25 to 74% in different regions of Turkey [24,26,28,29]. Bovine herpes virus-4 (BHV-4) is widespread in cattle populations around the globe. The virus has been frequently isolated from healthy cattle and from cattle with a wide variety of clinical signs such as nasal discharge and coughing. The BHV-4 seroprevalence in cattle ranges between 20.22 and 84.37% in Turkey and some other countries [29-31].

Malignant catarrhal fever (MCF) is a serious and fatal, disease that affects many species including cattle,

Table 1. Information about the cattle sector, farmers, quarantine, disease control, tests and cattle vaccinations in Turkey. The data on cattle population is taken from the Turkish Statistical Institution (TUIK) and the disease information is from the Ministry of Agriculture and Forestry.

Information about cattle diseases, farms and farmers in Turkey	
Total cattle population	18 million
Farms with > 500 cattle	There are 138 farms with > 500 cattle and a total of 113,000 cattle in these farms.
Literacy of the farmers	All farmers including the small family farmers can read, write and speak in Turkish. Some of the farmers in integrated farms know English and Turkish.
Training of the farmers on infectious diseases in cattle	Veterinarians organize seminars and specific training courses for farmers on disease prevention and control. A hand book on diseases and prevention was prepared by the Government (Ministry of Agriculture and Forestry-MAF). An European Union program on LSD was organized to make the farmers aware about LSD, prevention and vaccination. In addition, vaccine and other medical suppliers organize discussions with farmers.
Quarantine period and center	Quarantine period is for 3 weeks and every farm has a separate quarantine center.
Tests for the diseases	10% of the cattle are tested for IBR, BVDV and Blue tongue and the farmers pay for the test expenditure. In addition, Governmental organisations and veterinarians conduct routine tests for viral pathogens such as FMDV and LSD. and the farmers do not pay for this routine testing.
Diseases that are planned for the eradication	LSD and FMDV prevention and eradication measures are implemented by the Governmental organisations. Veterinarians practice specific preventive measures including vaccination and isolation for other diseases, especially BVDV and IBR.
Compensation	If an animal had notifiable diseases, the government pays 4/5 of the animal's total value.
Diseases that cattle are vaccinated against	Seasonal vaccination is organized for <i>Brucella</i> , FMDV, LSD, BVDV, IBR, BRSV, Rotavirus, Coronavirus, <i>E. coli</i> , Enterotoxemia, and <i>Pasteurella</i> . LSD and FMDV. Vaccines are administered by the Government for free.

bison, deer, moose, exotic ruminants and pigs. Malignant catarrhal fever virus (MCFV) belongs to the genus *Macavirus* of the family *Herpesviridae* (subfamily *Gammaherpesvirinae*). MCF in cattle has been reported worldwide including Turkey [32] indicating that MCF infections are common and need good management to reduce outbreaks. Vaccination is considered an effective method to prevent BHV-1 and reducing economic losses; however, it contributes to high seroprevalence. If the decision is made to eradicate the infection from cattle populations, the culling of seropositive animals without vaccination can be a successful method when the seroprevalence is relatively low. Previous reports indicated that some cattle that have recovered from an acute infection remain latent carriers for the rest of their lives, and the infection can be reactivated by stressful conditions and immunosuppressive treatments [23]. It is not possible to identify animals which have a latent BHV-1 infection with the currently available diagnostic tests. Alternatively, a well-planned vaccination program can be used to manage the disease. BHV is ubiquitous and highly contagious in nature. Vaccination is recommended as soon as passive immunity in calves has disappeared, usually around 3-5 months of age. Different types of vaccine are available against BHV-1, including modified live virus vaccines, inactivated vaccines, subunit vaccines, and marker vaccines. The timing of vaccination is at least as important as the choice of vaccine. Since maximum protection does not generally occur until approximately three weeks after vaccination, calves should be vaccinated two to three weeks before weaning at which time they are at risk of infection. A one-time vaccination will reduce the severity of disease, but will not provide complete protection and therefore booster dose is required. The use of marker vaccines is preferred since the antibody they stimulate can be distinguished from the antibodies that occur in natural BHV-1 infections. Currently, live BHV-1 vaccine is not approved for use in Turkey. Instead, inactivated marker vaccine or combined inactivated vaccines containing mixture of BHV-1, parainfluenza virus, bovine viral diarrhoea, bovine respiratory syncytial virus and bacterial strains are being used in Turkey. There are few options for combined vaccines containing different viruses and bacteria available commercially in Turkey.

Bovine respiratory syncytial virus infections

Bovine respiratory syncytial virus (BRSV) is an economically significant pathogen of cattle that causes approximately USD 1 billion in losses annually due to death, reduced performance, and cost of vaccinations

and medical treatment worldwide [33]. BRSV belongs to the genus *Orthopneumovirus* in the family *Pneumoviridae* and is a part of the bovine respiratory disease complex (BRDC) along with BHV-1, BVDV, bovine parainfluenza virus 3 (BPIV3), adenovirus, respiratory coronaviruses and other bacterial and fungal agents. Among dairy cattle, BRSV infection usually occurs in young calves aged between 2 weeks and 9 months. Adult animals with subclinical infection are the main source of infection and reinfections are common in herds. Direct contact is required for the spread of the BRSV. The virus is transferred from an infected cow through aerosols or droplets produced while breathing, coughing or sneezing. BRSV has been detected in cattle herds worldwide, with rates of infection that depend on management practices.

Several investigations have detected BRSV antibodies in cattle in Turkey [22,34-36]. The highest seropositivity of BRSV was 94% [35]. Serological studies on BRSV have been conducted in different geographic regions of our country. In these studies, percentage BRSV prevalence was 73% [32], 26.6% [36], 62% [37], 78.2% [38], 67.3% [39], and 46% [40]. Recently, Turkish BRSV strains were found to be closely related to the genetic subgroup III (subgroup A) of BRSVs reported from Brazil and America [44,55]. Live animal imports and mutual trade with these countries could be a possible reason for this association. Surprisingly, BRSV strains isolated from Turkey were not related to European BRSV strains indicating that there is no geographical transmission from neighbouring European countries. However, detailed phylogeographical investigations are needed.

The high serological prevalence of BRSV among Turkish cattle herds highlights the importance of further research on this infection; BRSV is not currently considered to be an important cattle disease in Turkey, mainly due to the lack of molecular diagnosis in the past. Multiple BRSV vaccines (killed and modified live) are commercially available and are generally administered as part of multivalent products. Calves vaccinated with the deletion mutant exhibited a robust virus specific antibody and CD4 T-cell response and were protected against virus infection [33]. Currently, combined vaccines containing BRSV and a mixture of other viruses (bovine herpes virus 1, parainfluenza virus, bovine viral diarrhoea) and bacterial strains are used in Turkey to protect calves from BRSV and BRDC. These vaccines contain the inactivated virus; however, a combined vaccine containing live BRSV was approved for use recently.

Bovine parainfluenza-3 virus infections

Bovine parainfluenza virus type 3 (BPIV3) is one of the most important pathogens in the bovine respiratory disease complex (BRDC). BPIV3 or bovine respirovirus is an enveloped, single-stranded, negative-sense RNA virus belonging to the *Respirovirus* genus in the family *Paramyxoviridae*. Like other respiratory pathogens, BPIV3 is transmitted via respiratory secretions through direct contact or inhalation of respiratory droplets. Sick animals show typical respiratory symptoms such as high fever, cough, nasal discharge and occasional bronchopneumonia.

Several BPIV3 serological studies were previously conducted in different geographic regions of Turkey. In these studies, the percentage values for BPIV3 prevalence were 43% [32], 44.6% [36], 44.6% [37], 85.6% [38], 18% [39] and 53.9% [40]. These studies were conducted either countrywide [37] or in selected regions [32,40]. Recently, a study revealed the presence of BPIV3 subtype C in Turkish cattle herds [41]. Currently, combined vaccines containing BPIV3 and other viruses (BHV-1, BPIV, BVD) and bacterial strains are being used in Turkey to protect calves from BPIV3 and BRDC. These vaccines contain the inactivated viruses, however, a combined live virus vaccine containing BPIV3 was licensed recently.

Bovine influenza D virus infections

Influenza D virus (IDV) can trigger bovine respiratory disease (BRD) complex and has been frequently detected in recent years [9]. However, data on IDV in Turkish cattle is limited. In a study conducted on cattle, nasal swabs and tissue samples from cattle in Marmara, inner Anatolia and Aegean region of Turkey were analyzed for the presence of IDV-RNA. Among the 76 samples from 12 cattle herds, IDV was detected in 3 cattle belonging to one herd. Sequencing and phylogenetic analysis of partial hemagglutinin esterase fusion (HEF) gene showed that the Turkish strain is 95% identical to its European and US counterparts, which suggests intercontinental spread of the virus [9]. However, comprehensive investigations are necessary in different regions of Turkey to identify the viral genotypes that are present.

Bovine coronavirus infections

Bovine coronavirus (BCV) belongs to the family *Coronaviridae*, and has a single-stranded, positive-sense RNA genome. BCV infection causes calf diarrhoea (CD), winter dysentery (WD) in adult cattle, and BRDC in cattle of all ages. Economic losses can be heavy due to a marked reduction in milk yield and

deaths. BCV cause severe respiratory and gastrointestinal infections affecting the animal breeding industry in Turkey and worldwide [42,43]. In a study conducted in Turkey, prevalence of bovine coronavirus infections was reported as 28.1% [43]. Pregnant cows are vaccinated to enhance the level of maternal antibodies that are transferred to their offspring through colostrum and thereby protect the newborn calves from BCV enteric disease. Intranasal administration of a modified-live virus (MLV) vaccine prepared with an enteric BCV was found to significantly reduce the risk of BCV in vaccinated animals. However, live vaccine is not approved for use in Turkey. Combined inactivated vaccines of bovine rotavirus, bovine coronavirus and bacterial strains are administered to the pregnant cows in the 3rd trimester of pregnancy.

Bovine rotavirus infections

Neonatal diarrhea in calves is an important disease, which causes economic loss due to high mortality and morbidity [44]. Bad managemental practices lead to increase in calf mortality. Bovine rotavirus (BRV) is one of the major causative agents of neonatal diarrhea in calves worldwide. The genome of rotavirus consists of segmented double stranded RNA, and is classified within the *Reoviridae* family.

In Turkey, rotavirus infections are significantly associated with calf diarrhea [44,45]. Both G and P bovine rotaviral types have been reported in Turkey. A recent study reported circulation of G8 BRV strains in Turkish sick calves and showed close association with European BRV strains [44]. Vaccines containing BRV antigens are commercially available and commonly used to prevent BRV diarrhea in young calves worldwide including Turkey. Inactivated combined BRV vaccines containing type G6 and G10 VP7 antigens are administered to calves. These vaccines are also administered to pregnant cows in the 3rd trimester of pregnancy.

Bovine norovirus infections

Bovine norovirus (BNV) is an RNA virus that belongs to the genus *Norovirus*, Family *Caliciviridae*. It is an important cause of diarrhea in calves and has been reported in several countries including Turkey [7]. Transmission of BNV occurs mainly through the fecal-oral route and direct contact. The prevalence was reported between 3.93-33.5% [7,46,47]. No vaccines are currently available for BNV.

Bovine viral diarrhoea

Bovine viral diarrhoea (BVD) is one of the most economically important diseases of the cattle industry worldwide. The monetary impact of the disease on cattle from around the world vary from USD 33 to 98 per cow [48]. The causative agent is bovine viral diarrhoea virus (BVDV), which is a *Pestivirus*, a group of small-enveloped RNA viruses belonging to the family of *Flaviviridae*. BVDV has spread worldwide in cattle populations and can cause repeat breeding, embryonic death, abortion, still births and congenital defect in infected pregnant cattle. BVDV is transmitted through a congenital infection of the fetus or after birth. Congenitally infected fetuses that survive in utero infection may be born as BVDV-infected calves. The BVDV infection in these calves will persist during the entire life of the calf, and they will shed BVDV continuously in the farm environment. These persistently infected calves should be determined and removed from the herd [3,48].

BVDV infections are common in Turkey [3,49,50]. The seroprevalence rates in cattle vary between 46–86%. About 0.07–4.9% of the animals were reported to be persistently infected in Turkey [3,49-52] and all BVDV genotypes (BVDV-1, BVDV-2 and BVDV-3) have been reported [3,52]. The Turkish BVDV-1 isolates have been characterized into BVD-1L and BVD-1R based on phylogenetic analysis [3,50-52].

Vaccines for BVD control are available worldwide and grouped into two categories: modified live virus vaccines and killed virus vaccines. In general, modified live virus vaccines require only one dose during the initial immunization step, however they are more difficult to handle and require strict refrigerated conditions for shipment. Killed vaccines are usually more expensive due to multiple dose requirement during immunization. However, killed virus vaccines are less susceptible to deactivation by temperature extremes and chemicals. Recently, a modified live virus vaccine containing attenuated virus was approved in Turkey. Currently, commercially available combined inactivated vaccine for the control of BVDV (composed of subgenotype 1a, NADL strain), BHV-1, BPIV-3 virus, BRSV and bacterial strains are being used in Turkey. Inactivated vaccines containing only Bega and Trangie strains of BVDVa and C-86 strain of BVDVb are also available and are used regularly in Australia and New Zealand respectively [48].

Bovine adenovirus infections

Bovine adenoviruses (BAVs) are non-enveloped double stranded DNA viruses and belong to the

Atadenovirus genus of the family *Adenoviridae*. BAV infections result in a variety of clinical symptoms including conjunctivitis, pneumonia, diarrhoea, and polyarthritis. Bovine adenoviruses are found worldwide and are particularly widespread in Central America and Africa. BAVs are shed in respiratory and fecal secretions and thus inhalation and ingestion routes could play a key role in their transmission [53,54].

Öztürk and Toker determined the presence of antibodies against BAV-1, 2 and 3 in blood serum of 214 cows in Turkey by mNT [53]. They found seropositivity rates of 71%, 84% and 89% for BAV-1, 2 and 3, respectively. Alkan *et al.* reported lower seroprevalence rates for BAV-1 (23.7%), BAV-2 (35.2%) and BAV-3 (12.0%) type infections in cattle in Turkey [54]. The results of the aforementioned studies indicate that bovine adenoviruses are present in Turkey.

Both modified live and inactivated adenovirus vaccines have been developed and evaluated for use in cattle and they are administered when maternal antibodies have waned. Most vaccines are formulated in combination with other agents. Two to four doses of the vaccine administered subcutaneously or intramuscularly are recommended to provide adequate protection. Vaccination has not eliminated the infection entirely, but has resulted in reduction in disease incidence and treatment costs. However, vaccination against BAV is not being practiced in Turkey.

Bovine leukosis

Enzootic bovine leukosis (EBL) is a disease caused by bovine leukaemia virus (BLV), an oncogenic retrovirus belonging to the family *Retroviridae* and genus *Deltaretrovirus*. The disease has a long incubation period and is characterized by persistent lymphocytosis, leukaemia, and/or tumours. Economic losses from BLV infection are mainly due to reduced milk production, decreased reproductive performance, increased replacement costs, veterinary costs and labour requirements. The main routes of transmission are surgical manipulations, infected needles, and blood-sucking insects. However, small proportion of infections may occur by vertical transmission, in utero, or through colostrum and milk [55,56]. In Turkey, EBL has been listed as a notifiable disease since 2011, and quarantine and serological diagnosis methods have been used to control the disease.

BLV infection with seroprevalence up to 67% has been reported in some regions in Turkey [55-59]. Most of these studies were based on public farms. However, serosurvey studies indicated that, rate of the infection was lower in private farms [55-59], possibly due to

better management and biosecurity practices. At present, there is no commercial vaccine available for BLV.

Schmallenberg virus infections

Schmallenberg virus (SBV) is a Shamonda/Sathuperi like RNA virus which belongs to the Simbu serogroup of the genus *Orthobunyavirus* in the family *Peribunyaviridae* and is transmitted through biting midges. SBV is a novel virus that has been found to cause abortions in cattle in European countries and Turkey [60-63]. Azkur *et al* reported overall seroprevalance of 24.5%, 39.8%, 1.6%, 2.8%, and 1.5% in cattle, sheep, goats, and Anatolian water buffalo, respectively [60]. Yilmaz *et al* detected SBV through reverse transcriptase polymerase chain reaction (RT-PCR) in aborted fetuses of sheep, goat and cattle from Marmara region of Turkey [62]. Genotype analyses have shown that the strains found in aborted fetuses were similar to those previously reported in Germany [61]. The presence of SBV-RNA was detected in 6 (3.3%) samples from cattle herds in Central Anatolia, Turkey in 2013 [63]. In addition, SBV-specific antibodies were detected in 87 (24.1%) of 360 sera using a virus neutralization test [63]. No vaccines are currently available.

Lumpy skin disease

Lumpy skin disease (LSD) is a highly contagious, transboundary and notifiable disease of economic importance in cattle. The lumpy skin disease virus (LSDV) is a dsDNA virus belonging to the genus *Capripoxvirus* and family *Poxviridae*. LSDV is primarily transmitted by arthropod vectors but other routes cannot be excluded. Clinical signs occur at the cutaneous (firm nodules) and subcutaneous (oedema) levels. These lesions can also appear in other tissues such as the respiratory, digestive and genital tracts, and the lymph nodes [64].

LSD is currently endemic in most areas of Africa and parts of the Middle East including Turkey. LSD was endemic in Turkey until 2017. It has been sporadic lately after intensive and effective vaccinations. Outbreaks also occurred recently in parts of Asia, a few Causasian countries, and in Europe particularly in the Balcan countries. Although the lumpy skin disease was eradicated from some of the affected countries, it continues to be present in some others. LSD is currently endemic in Turkey [64]. The first reports of LSD in south-eastern Turkey were in mid 2013 in the city called Kahramanmaras. South-eastern and eastern Turkey share about 1,300 km border with neighboring

countries: 911 km with Syria and 384 km with Iraq. After the first outbreak, several outbreaks occurred in the south-eastern, eastern and central Anatolia, Mediterranean, Aegean, Marmara and Black Sea regions of Turkey. The number of outbreaks was 784 and 510 in 2014 and 2015 respectively. In 2016, the number of outbreaks and cases were decreased after the control measures taken by the Ministry of Food Agriculture and Livestock of Turkish Republic [64,65].

Recent studies [66,67] indicated that LSD isolates clustered together with African and Middle east LSD isolates. The precise origin of the LSD virus responsible for the outbreaks in Turkey is unknown. However, it is possible that the disease was introduced into the country by infected cattle trafficked from Iraq and Syria and spread via arthropod vectors. More than three million Syrian refugees have crossed into Turkey in recent years after the political conflict and they came with their belongings including animals. After the 2011 civil war in Syria, more than three million Syrian refugees crossed into Turkey and came with their belongings, including animals. The uncontrolled movement of infected animals may be the main factor in the spread of disease throughout various regions of Turkey. There is no available data regarding LSDV in Syria due to the civil war; however, the infection has been endemic in Iraq, Iran, Egypt, Jordan, Israel, Yemen, Sudan and Saudi Arabia during the last three years. The disease was reported in Greece in August 2015. In 2016, it spread through different Balkan countries (Bulgaria, Former Yugoslav Republic of Macedonia, Serbia, Kosovo, Albania and Montenegro) and Caucasian contries (Azerbaijan, Goergia and Russia) [64-67]. It is likely that this disease will spread to the other European countries. A HORIZON 2020 project (DEFEND) has recently begun to prevent and control LSD in European countries.

Investigations on the risk assesment, hosts, host immunity and vaccination strategies are needed for LSD. The implementation of appropriate biosecurity measures in herd management could also reduce infection rates and economic losses incurred by farmers. Awareness campaigns for farmers and veterinary staff to improve identification of LSD should be considered. Turkey should work together with the neighbouring countries to prevent the spread of the disease across national borders [64]. Mitigating strategies including vaccination, biosecurity and vector control have been in practice since the disease was first seen in Turkey in 2013. However, these strategies must be adopted by all neighbouring countries to control LSD in countries where it is endemic.

In Turkey, quarantine, culling, restriction of animal movements, disinfections, vector control and especially vaccination have been found to be effective ways to control LSD [64,65]. Five doses of live attenuated sheep pox vaccines have been used in Turkey resulting in dramatic decrease in disease incidence. Live, attenuated virus (SIS Neethling-type) vaccine (Lumpyvax, MSD) is being used in some other countries for immunization against LSDV [64,65,66]. In general, vaccine reactions as well as vaccine failures have been observed. More data and analyses are needed to determine the dose and detailed effect of sheep pox vaccination against LSD in Turkey. Data indicate that there have been some cases of disease outbreak in the vaccinated regions. This might be because some farmers did not vaccinate their cattle during the epidemics or due to lack of individual immune response to vaccine [64]. Therefore, farmers' awareness about vaccination is very important in controlling LSD along with rapid diagnosis and biosecurity [64,65].

Pseudocowpox

Pseudocowpox virus (PCPV) infects cattle throughout the world and has zoonotic potential. PCPV is a member of the genus *Parapoxvirus* that infects vertebrates, and is classified into the family *Poxviridae*. PCPV is usually transmitted within herds by direct contact between animals or indirectly through exposure to contaminated surfaces and/or equipment. Infection with PCPV can affect cattle of all ages, but is more common in younger animals. Lesions are generally located on the lips, in the oral cavity, and/or on the muzzle in younger animals, and on the teats and udders in older cows. PCPV was detected and characterized in cattle in Turkey a few years ago [68]. The importance of PCPV is increasingly recognized in Turkey, primarily because of the economic losses to farmers in connection with the disease outbreaks and because of its zoonotic potential. There is no commercial vaccine available against PCPV.

Epizootic hemorrhagic disease

Epizootic hemorrhagic disease (EHD) is caused by epizootic hemorrhagic disease viruses (EHDVs). These are orbiviruses transmitted by *Culicoides* biting midges to domestic and wild ruminants. EHDVs are dsRNA viruses (genus *Orbivirus*, family *Reoviridae*). The EHDV serogroup consists of 7 provisional serotypes occurring worldwide including Africa, North America, Australia, Japan, and Israel [69]. EHDVs generally exist in temperate and tropical climates that support the vector populations.

An EHD outbreak occurred in Turkey in 2007. Phylogenetic analysis indicated that the virus belonged to EHD virus serotype 6 [69]. Albayrak *et al* [70] found precipitating antibodies against EHDV in 3.5% of 399 bovines and 2.43% of 82 gazelles (*Gazella subgutturosa subgutturosa*) serum samples collected from Aegean, Black Sea and southeastern Anatolia regions of Turkey.

Bovine ephemeral fever

Bovine ephemeral fever (BEF), also known as three-day sickness or three-day fever is an arthropod-borne viral disease that mainly affects cattle and water buffalo. BEF infection was first reported in the mid-nineteenth century when the disease was first observed in East Africa [71,72]. The etiological agent of this disease is bovine ephemeral fever virus (BEFV), a member of the genus *Ephemerovirus* within the family *Rhabdoviridae*. BEFV consists of a single-stranded RNA genome and 5 nonstructural proteins. BEF causes economic losses by a sudden drop in milk production in dairy cattle and loss of condition in beef cattle. Although mortality resulting from this disease is usually < 1%, it can occasionally be \geq 20%. BEF is distributed across many countries in Asia, Australia, Middle East and Africa. Prevention and control of the disease is mainly through regular vaccination. The impact of BEF on the cattle industry may be underestimated, and the introduction of BEF into European countries is possible in the same way as the spread of the bluetongue and Schmallenberg viruses. Research on BEF remains limited and priority of investigation should be given to defining the biological vectors of this disease and identifying virulence determinants [71,72].

The first report of ephemeral fever in Turkey was published by Girgin *et al.* [73]. They reported a clinical disease with pathognomonic changes in cattle during an outbreak in 1985 in the central, south and south-eastern parts of Anatolia. The mortality rate in the 1985 outbreak was < 2% [73]. After the first report, at least five outbreaks (1996, 1999, 2005, 2008 and 2012) were reported in the southern/south-eastern region, and the last outbreak was observed in 2012 [74,75,76].

The last outbreak in 2012 began in Adana, Turkey; more than 20,000 cattle in southern and south-eastern Anatolia (36°00'N–37°00'N), were affected. A total of 2074 animals died or were destroyed, and 763 were referred for slaughter by veterinarians (http://uluderetarim.gov.tr/haberler-287-Uc_gun_hastaligi.html) in more than 250 villages and 800 farms in Turkey. The mortality rate was higher than

that observed in the previous episodes [74]. The molecular characterization of BEFV from Turkey was reported for the first time on the basis of the G gene that was partially characterized from the strain that caused the 2008 outbreak [74]. Recently, the sequencing of BEFV strains from the 1985 and 2012 outbreaks have been reported [75,76]. BEFV can survive the winter in insect vectors. In addition, new BEFV variants may travel from one country to another by wind or through livestock trade. Currently, there is no commercial BEFV vaccine produced or imported in Turkey. Vaccination for population immunity and prevention of transmission by a number of dipteran vectors have been the main methods for the control of BEFV infection [71,74].

Unfortunately, the origin of the BEFV that caused the last outbreak is not clear. In the past decade, a large number of animals were imported to our country from Australia, and South American and European countries. According to the Australian livestock export industry, there is animal movement from Australia to Turkey and also to Far-Eastern countries such as China, and Middle Eastern countries such as Egypt, Israel and Saudi Arabia (<http://www.mla.com>). Animals are quarantined when they arrive in Turkey before they are sent to the farms (Table 1). Besides, religious festivals increase animal movement in our country every year. In addition, the possible increased vector population due to climate change in the last two decades may be an important risk factor for BEF dynamics in Turkey.

Bovine rabies

Rabies is a zoonotic, fatal and progressive neurological infection caused by a neurotropic, negative sense, non-segmented, single-stranded RNA virus that belongs to the genus *Lyssavirus* of the family *Rhabdoviridae*. It affects all warm-blooded animals and the disease is prevalent throughout the world and endemic in all countries except in islands like Australia and Antarctica. It is transmitted by saliva through bites and scratches of infected mammals. The infection primarily circulates among domestic, feral, and wild animals such as dogs, cats, monkeys, foxes, bats, raccoons, and skunks, although all mammals are at risk [77].

Turkey has a well-developed surveillance system for diagnosing rabies and has made repeated attempts to eliminate the disease. However, rabies persists in Turkey in the form of both dog-mediated and fox-mediated rabies. Wildlife rabies appears to represent a greater risk to cattle than dog-mediated rabies in Turkey, and dog rabies remains a problem in villages.

On average, 85 rabies cases in cattle were reported annually in Turkey between 2008 and 2011. Incidence in the Aegean region was higher than other regions. The rabies situation in the Black Sea, Mediterranean and south-east Anatolian regions is dominated by dog-mediated transmission with suspected self-limiting spillover infections in wildlife species such as foxes and golden jackals. Wildlife rabies (via wild canines) in Turkey has led to increase in the number of rabies cases in cattle. During 2008-2011, numbers of confirmed bovine cases from Turkey ranged from 1 to 5 per 100,000 animals [78]. The degree of underreporting in Turkey may be influenced by incentives to submit samples. In the western part of Turkey many farmers have animal insurance policies and therefore, rabies suspected animals especially cattle can be submitted for testing. In the less affluent eastern part of the country, most farmers do not have insurance and consequently farmers will be less likely to submit livestock for rabies diagnosis. Since 2012, the Turkish government initiated a compensation scheme for farmers. Confirmed bovine cases indicating economic losses are not substantial, but these costs could escalate rapidly if control measures are not put in place to prevent further spread of fox-mediated rabies [78]. Rabies vaccines that are approved for animal use consist of the live attenuated virus (e.g., Flury high egg passage, Flury low egg passage, Street-Alabama-Dufferin and Kelev), chemically or physically inactivated virus and recombinant vaccines. More advanced vaccine types could be developed to nullify the drawbacks of conventional vaccines. There is a need to enhance surveillance for rabies virus variants currently circulating in animals, especially in wildlife. The role of wild animals in the transmission of rabies in Turkey is not clearly understood. Public awareness on rabies transmission can play a major role. High-level political commitment is also essential to accomplish these recommendations.

Future challenges and prospects regarding the control of major viral diseases of cattle in Turkey

The Turkish milk and meat sector has great potential and Turkey is one of the largest producers of milk and dairy products in the region. Management of the health of cattle is a prerequisite for profitable cattle production. Determination of farm management practices is of paramount importance when evaluating the epidemiology of livestock diseases and farm profitability. It is also well documented that considerable financial losses in the livestock sector are associated with losses due to diseases and faulty

management practices. New investments in the Turkish dairy and meat sectors for an organized health care system of animals need to be encouraged. Personal communications and research reports from various regions of the country indicated that viral diseases in cattle are a growing threat to the Turkish cattle industry. Viral diseases are regularly causing serious losses to farmers. Moreover, live animals are imported to Turkey from several countries, especially from the neighbouring countries, and adherence to strict quarantine measures are of utmost importance to minimize the entry of new pathogens into Turkish cattle herds. Sporadic outbreaks of various infectious diseases in village cattle herds are reported in Turkey, possibly due to lack of vaccination practices and also due to lack of awareness and education among these communities. These village cattle herds are a potential source of pathogen spread to commercial cattle. In addition to this, most cattle owners with only a few animals may not vaccinate their animals resulting in incomplete and inefficient application of disease preventive strategies.

Another issue is the difficulty in controlling animal movements from the neighbouring countries, either due to political conflict (like Syria and Iraq) or illegal trade. Turkey shares its border with 8 countries (Georgia, Armenia, Azerbaijan, Iran, Iraq, Syria, Greece, and Bulgaria) and it is difficult to control animal movement across borders; this leads to spread of the pathogens between European countries, the Middle East, and Asia. The authorities in the meat and milk sector in Turkey, the Middle East and in European countries should work together and implement appropriate control strategies for viral diseases in this region. This issue has been addressed by the horizon 2020 project (DEFEND) that has resulted in control and eradication of LSD in this region.

The Turkish cattle industry is refining its strategies and policies to mitigate viral infections in cattle herds on the basis of available research and field observations. Correct diagnosis of viral diseases and epidemiological studies will help decide on implementation of prevention and control strategies to combat viral infections in Turkish cattle. Farmers can significantly reduce spread of infections and economic losses through timely and precise diagnosis and by adopting quarantine and preventive measures; thus, leading to enhanced productivity and biosafety. Proper vaccination plays a key role in the prevention and control of many economically important viral diseases of cattle. Vaccines are still the best choice for inducing protective responses; however, vaccines are not available against all viral infections and the efficacy of

vaccines for some diseases is variable. Size of cattle herds, quality of application procedure, health status of animals and farm management may influence vaccination practices in Turkey. Most of the poor or village farmers may not vaccinate their animals either due to high costs of vaccines or lack of awareness. This leads to failure to follow integrated programs for the prevention of predisposing pathogens and eventually leads to failure of the respective vaccines. In addition, improper handling and application of live vaccines at farm levels could also lead to vaccination failure. Therefore, veterinary authorities and government policy makers should prioritize training of farmers and provide the best possible incentives for vaccination. Moreover, local vaccine production companies and research institutes should be supported and encouraged to produce vaccines within Turkey in order to lower the cost of vaccines. At present, there are only a few local vaccine companies (Vetal and Dolvet) as well as the Government Veterinary Institutes that produce vaccines for animals.

Funding for scientific research related to the economic aspects of the Turkish cattle industry are not adequately available. The funds allocated for research and skills development should be increased. These shortcomings are hindering the implementation of efficient vaccine research programs. Furthermore, cost of imported vaccines and continuous emergence of new viral variants due to virus genetic evolution are also creating hurdles for cattle farmers. There is a clinical need for updating some commercial vaccines due to the newly emerged virus strains. For this, viral strains need to be monitored by scientific investigations performed by the universities and veterinary institutions.

Regulatory commitment and release of funds for disease management programs and motivation to work in disease control programs are needed for successful eradication of livestock diseases in Turkey. Turkish consumers are very sensitive about food safety and have had negative experiences in the past due to BSE in Europe and avian influenza in Turkey. Therefore, disease investigation and control programs in Turkey need special attention from veterinary authorities, veterinarians, government, and policy makers. In order for the eradication to be successful, compulsory control measures are needed and legislation that requires cattle testing by reluctant farmers should be implemented (Table 1). Diagnostic testing may need to be paid for by the farmers and subsidies should be given to farmers to encourage their participation in disease control programs (Table 1). There is a dire need for better infrastructure, knowledge, diagnostics, regulations and

policies for disease eradication in cattle in Turkey. Currently, the Ministry of Agriculture and Forestry, General Directorate of Protection and Control is working towards disease prevention control and eradication in collaboration with the Veterinary Faculties.

This review summarises published data on different aspects of cattle diseases in Turkey and highlights the knowledge gaps and vaccination scenarios in commercial cattle farms (Table 1). There is a critical need for well organised diagnostic laboratories and reporting systems throughout Turkey in order to improve our knowledge on cattle diseases, and for better implementation of control measures. In addition, application of Polymerase Chain Reaction (PCR) based assays in every diagnostic laboratory can significantly increase our understanding of the epidemiology, dissemination, diagnosis and vaccine control of cattle viral diseases in our country. Further studies are necessary for monitoring the viral strains circulating throughout Turkey to design better vaccines and immunization protocols against devastating viral diseases. Furthermore, veterinarians and farmers should be informed about the pathogens that are circulating in their region and educated on the use of efficacious vaccines. Vaccines should also be regularly updated based on circulating field strains.

The cattle production sector was negatively impacted by the SARS CoV-2 pandemic. Therefore, government, farmers, veterinarians, and researchers should come together not only at national level but also internationally to solve the problems faced by the cattle industry.

Acknowledgements

We would like to thank the University of Istanbul-Cerrahpasa for providing funds for some of the studies (cited in this review) at the Department of Virology, Istanbul University-Cerrahpasa. Partial funding for this study was provided through grants from the Center on Emerging and Zoonotic Infectious Diseases (CEZID) of the National Institute of Health under award number P20GM130448.

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Conflict of interests: No conflict of interests is declared.