PREVALENCE, DIAGNOSIS, MANAGEMENT AND CONTROL OF IMPORTANT DISEASES OF RUMINANTS WITH SPECIAL REFERENCE TO INDIAN SCENARIO

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ABSTRACT

India possess huge livestock population, which is endangered by different endemic infectious diseases (bacterial, viral, protozoan and parasitic), which collectively causes significant economic losses to the landless poor farming community. Infectious diseases impose economic losses by causing morbidity, mortality, decreased production (milk, meat, wool etc.), decreased feed conversion ratio which results in reduced weight gain, decreased draught power and fertility. Furthermore, economic burden is also due to the cost of treatment, abortion, consequences on internal livestock movement, germplasm and international trade. In addition, some of the diseases are zoonotic and inflicts considerable impact on public health. Uncertain agrarian climate, unpredictable weather, drought, floods, migration of livestock, scarcity of fodders, and unhygienic zoo-sanitary and healthcare practices together resulted in endemicity of diseases ultimately leads to more incidence and prevalence of livestock and poultry diseases throughout the year. Synchronized monitoring and surveillance of disease throughout the country is a fundamental requirement for sustainable livestock production. With fairly developed telecommunication in India, following technologies like interactive voice response system, SMS through mobile/cell phones and toll-free landline phones (voice mail) are required for enhancing the effectiveness and efficiency of

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disease monitoring and surveillance. Multidisciplinary approaches at international, national and local levels are required for management, control and eradication of endemic and transboundary diseases of livestock. Improved monitoring and/or surveillance, rapid and confirmatory diagnosis, and networking of diseases are required to go forward in the path of eradication. Vaccination is the main strategy for control and eradication of many diseases. Good management practices consisting of stringent biosecurity measures, strict sanitation and hygiene practices in the farm, isolation and quarantine of diseased animals, and trade restrictions are necessary for successful operation of control programmes. This review highlights prevalence, pathogenesis, diagnosis, and prevention and control measures for important diseases of ruminants with special reference to India.

1 Introduction

India possesses rapid growing animal husbandry sector and moving towards to attain self-sufficiency in the production of livestock products (Dhama et al., 2014a). The animal husbandry department is a major contributor to the Indian economy and overall contribution is 28-32% in agricultural GDP and 4 to 6% of the national GDP. It also contributes 8-10% of the country's labour power (Hemadri & Hiremath, 2011). India possess largest livestock population in the world with 528 million of domesticated animals; first place in the world in buffalo population (105.3 million), second in cattle (199 million) and goat (140.5 million) population, and third in sheep (71.5 million) population (Hemadri & Hiremath, 2011; Biswal et al., 2012; Dhama et al., 2014a; Chand et al., 2015). Livestock population in India is threatened by disease outbreaks, droughts, floods and other climatic anomalies.

There are several diseases affecting livestock that causes serious effect on the production of animals, human health, trade of livestock and animal products, as a result the overall economic development will be affected (Gibbs, 1981; Depa et al., 2012; Dhama et al., 2014a). Improved quality and quantity of livestock products is necessary, in order to compete in the international market, which intern needs disease free animal health status (Bhanuprakash et al., 2011; Awase et al., 2013; Bayry, 2013; Chand et al., 2015). In recent times, emerging and re-emerging diseases of livestock, poultry and humans have tremendously increased. Many of the diseases like brucellosis, tuberculosis, glanders, corona, influenza, Nipah and Hendra viral diseases are of zoonotic significance (Chakraborty et al., 2014; Dhama et al., 2014a; Kumar et al., 2015a).

Beside that several other viral diseases of animals in India such as foot and mouth disease (FMD), bluetongue (BT), peste des petits ruminants (PPR), sheeppox, goatpox, camelpox, infectious bovine rhinotracheitis (IBR), malignant catarrhal fever (MCF) and bacterial disease like haemorrhagic septicaemia (HS), black quarter (BQ), anthrax and brucellosis were endemic and has potential of crossing continental boundaries (Arya & Bhatia, 1992; Benkirane & De Alwis, 2002; Bhanuprakash et al., 2011; Biswal et al., 2012; Saminathan et al., 2013; Bayry, 2013; Chand et al., 2015; Kumar et al., 2015a). Emergence of new serotypes in various pathogens creates additional risk and warning to the livestock

and human population. Higher occurrences of emerging and re-emerging diseases might be due to various factors like crowded livestock and human population, deforestation, lack of public awareness and increased contact between livestock and humans with wild animals and birds (Depa et al., 2012; Chakraborty et al., 2014). The global expansion of cultivating land, population growth, intensive industrialization, climate changes, movement of vectors, illegal and unregulated trade, hiding/reduced reporting of the disease outbreaks are other reasons for the emergence and spreading of the disease (Gibbs, 1981; Dhama et al., 2014a). Two-thirds of the global population including human and livestock are living in the developing countries and majority of the diseases were emerged from developing countries. International and national collaboration along with sincere scientific implementations and political decisions are necessary to tackle such emerging infectious diseases (Bhanuprakash et al., 2011; Hemadri & Hiremath, 2011; Biswal et al., 2012).

An effective management for emerging and re-emerging diseases needs multidisciplinary activities like surveillance, rapid reporting, collection and transport of clinical materials for diagnosis of the etiological agents, strengthening of basic research, epidemiological modelling and prediction, forecasting model development, development of novel vaccine candidates and suitable adjuvants etc. (Biswal et al., 2012; Depa et al., 2012; Chand et al., 2015). The present review discusses the prevalence, pathogenesis, diagnosis and prevention and control measures for important diseases of ruminants with special reference to India.

2 Viral diseases of ruminants

2.1 Foot and Mouth Disease (FMD)

Foot and mouth disease (FMD) is endemic in India from 1864 onwards (Subramaniam et al., 2013). Animal population in India is threatened by FMD owing to unrestricted movements of animals, incomplete vaccinations, and inapparent infection in small ruminants which act as reservoirs. Direct loss of 20,000 crore/annum has been estimated due to the disease (Venkataramanan et al., 2006). FMD causes huge economic losses and decrease in milk yield causes 8% of total direct loss (Mathew & Menon, 2008). The other economic losses were huge expenditure spent for FMD control programmes throughout the country by the government, increased cost for

treatment, decreased productivity (meat, wool etc.) and draught power. The disease causes severe damage to the production and international trade. Because of its severity, the OIE and FAO declared it as “High Priority Disease”. The body also appealed to different countries to make effective groups for its strategic control (FAO & OIE, 2012). FMD affects wide variety of host including 529 million of livestock as well as captive and free-living wild even toed animals (Verma et al., 2008; Verma et al., 2012). Among 7 serotypes (O, A, C, Asia1, SAT-1, SAT-2 and SAT-3), only O, A, C, and Asia-1 were recorded in India. Since 1995, C serotype has not been reported from India and the globally the last outbreak was reported in Ethiopia during 2005 (Rweyemamu et al., 2008). About 70-80% of outbreaks are due to ‘O’ followed by Asia 1 (3-10%) and A (3-6.5%) (Hemadri & Hiremath, 2011; Biswal et al., 2012; Pattnaik et al., 2012). The FMD incidence is increased in India due to the execution of schemes for indigenous cattle genome improvement by cross-breeding of local cattle breeds with exotic cattle.

FMD incidences were more during pre-monsoon and winter season; however incidence of FMD were reported regularly all the months of year. The probable reason for its continuous persistence is due to uncontrolled animal movements throughout the country. Besides that because of the weak financial status of some of the livestock owners; their herd remains unvaccinated which poses additional threat to the surrounding vaccinated herds. It has been reported that among 10 genotypes of serotype A, only 2 called as VI and VII were circulating in India from past 20 years. In Asia 1 serotype, VIA and VIB genotypes were circulating in India (Verma et al., 2010; Hemadri & Hiremath, 2011; Biswal et al., 2012; Pattnaik et al., 2012; Subramaniam et al., 2013). The control and eradication of FMD in India, progressive control pathway (PCP) was implemented (Rweyemamu et al., 2008). The FMD control programme (FMDCP) was executed in 54 districts from 8 states of India during 10th five year plan (based on epidemiological data obtained from more than 35 years) covering the population of 30 million cattle and buffalos. In the control program implemented areas, there has been gradual build up of herd immunity and substantial fall in the disease incidence (Biswal et al., 2012; Depa et al., 2012; Pattnaik et al., 2012; Verma et al., 2012; Subramaniam et al., 2013).

2.2 Peste des Petits Ruminants (PPR)

Peste-des-petits-ruminants (PPR) is a highly contagious, acute and transboundary viral disease of goats and sheep caused by the genus *Morbivirus* belonging to the family *Paramyxoviridae*. Clinically, the disease is manifested as conjunctivitis, high fever, oculonasal discharge, necrotizing and erosive stomatitis, enteritis and bronchopneumonia followed by either mortality or recovery from the disease (Taylor, 1984). Currently, as South Asia is more focused for PPR, it percolates serious losses to the countries like Afghanistan, Pakistan, Nepal, Bangladesh and India. The disease was first observed in Tamil Nadu in 1987 (Shaila et al., 1989). On the genomic basis the virus is grouped into four

lineages i.e. I, II, III, and IV out of which lineage IV is common in Asia (Balamurugan et al., 2012). In India, till date, only lineage IV viruses have been reported. In North-eastern regions the seroprevalence rate of PPR in goats was 13.8% in Assam (Begum et al., 2016) and 2.11% in Tripura. The PPRV goat strain isolated during 2013 outbreak in Tripura region of India shared 99.2 to 99.6% nucleotide identities with the Bangladeshi strains (Muthuchelvan et al., 2014).

The disease outbreak is most commonly observed in the months of April to October followed by winters. Goats were more susceptible to PPR and manifest severe clinical form of disease than sheep. A report from central India showed occurrence of dual infection of PPR and Goatpox in indigenous goats (Malik et al., 2011a). Several PPR outbreaks were encountered and the disease is enzootic in most of the southern states of India like Karnataka, Andhra Pradesh and Tamil Nadu; western states of India like Maharashtra; eastern states of India like West Bengal and Orissa; northern states of India like Rajasthan and Himachal Pradesh; central states of India like Madhya Pradesh (Dhar et al., 2002; Balamurugan et al., 2012; Singh et al., 2013; Muthuchelvan et al., 2015). The expected yearly losses due to this disease may reach up to 1800 million rupees. In northern region of India, outbreaks were most frequent in goats whereas in southern regions of India, the outbreaks were most frequent in sheep (Balamurugan et al., 2012; Balamurugan et al., 2014). The economic losses per animal in sheep and goats ranges between Rs. 523 to 945 (Thombare & Sinha, 2009; Awase et al., 2013). The growth of goat industry is hampered by PPR owing to high morbidity (50-90%) and mortality (50-85%) rates. Kids more than 4 months and less than one year of age are more susceptible to PPR.

The occurrence of disease outbreaks was higher during March to June (51.7%) when compared to remaining months (Thombare & Sinha, 2009; Awase et al., 2013). The economic impact of PPR includes trade limitations; a hindrance to intensive livestock production development due to the impedance to the import of new breeds, which in turn cause scarcity of animal protein to humans. The control of PPR can be achieved by effective vaccination measures. Infected animals should be kept in quarantine for the period of one month. In the infected area, the movement of the animal should be restricted strictly. Practically, sanitary and control measures are difficult to follow in India due to vast nature and PPR endemicity. However, the effective measure for PPR control is mass vaccination using the effective vaccine, along with quarantine measures (Sen et al., 2010; Balamurugan et al., 2014; Muthuchelvan et al., 2015).

The control measures should contain the “bottom-up” approach such as from livestock owners to field veterinarians to policy makers (Singh, 2011). Further, increasing the production of PPR vaccine, enhancing the disease diagnostic facilities, strengthening the quality control units and improved infrastructure facilities for field workers is necessary for management and control of diseases. The NCP-PPR control

scheme was implemented in 2010 and presently extended to all the states of the country (Balamurugan et al., 2014; Muthuchelvan et al., 2015).

2.3 Bluetongue (BT)

Bluetongue (BT) disease is now endemic in India and the first case of BT was reported from Maharashtra during 1964 (Sapre, 1964). Later on, the disease has been reported from several parts of the country based on virus isolation and/or detection of BTV-specific antibodies. BTV belongs to the genus *Orbivirus* of the family *Reoviridae* (Pringle, 1999). In serological survey, the presence of antibodies against BTV in Indian cattle, buffalos, goats, camels as well as in some wild ruminants has been observed. However, in cattle and buffalos, clinical form of BT has not been reported. The clinical signs vary from asymptomatic to fatal form which is determined by the BTV serotype, animal species, breed and age (Elbers et al., 2008). Recently, 27 BTV serotypes have been identified worldwide with the addition of 2 more new serotypes (Maan et al., 2011; Zientara et al., 2014). In India, 22 serotypes have been recognised on the basis of virus isolation and/or serology (Rao et al., 2016). Presently, 13 serotypes namely, BTV-1, 2, 3, 4, 6, 9, 10, 12, 15, 16, 17, 18, 21 and 23 were isolated from India especially from southern states (Maan et al., 2012; Minakshi et al., 2012; Rao et al., 2012; Chauhan et al., 2014). Genomic studies of these serotypes exhibit their variation with the standard reference strain (Rao et al., 2016). *Culicoides* spp. is the major vector for BTV. Among 1400 species were identified worldwide, minimum 39 species have been identified as vector for BT in India (Maheswari, 2012).

The analysis of outbreak data reveals that the intensity of disease outbreak was severe in Karnataka followed by Andhra Pradesh and Tamil Nadu (Hemadri & Hiremath, 2011). During 2007-08, a severe outbreak of the disease was happened in India, afterwards only a mild clinical form of disease was observed (Hemadri & Hiremath, 2011). Diagnosis of BT can be done by epidemiology, vector species, clinical signs, post-mortem findings and molecular tests (Afshar, 1994). Confirmatory diagnosis can be done by virus isolation, detection of anti-BTV antibodies by serological methods and nucleic acid detection by RT-PCR. BTV can be isolated from chicken embryonated eggs and competitive ELISA (c-ELISA), virus neutralization test (VNT) and agar gel immunodiffusion (AGID) assay (Afshar et al., 1989; Pathak et al., 2008). By using RNA-PAGE, cell culture adapted Indian BTV with more than 10 segments have been reported (Ramakrishnan et al., 2005b). For successful control of BT in India, it is required to initiate vector and sentinel control measures and rapid disease diagnosis. The control measure for BT includes vaccination of animals with an inactivated BTV vaccine. Inactivated monovalent BT vaccines were developed using BEI (Ramakrishnan et al., 2006) and hydroxylamine inactivants (Ramakrishnan et al., 2005a). Recently, for control of BT in India, inactivated pentavalent vaccine consisting of BTV-1, 2, 10, 16 and 23 was developed and commercialised (Reddy et al., 2010). Control of BT in India is a difficult task due to more

susceptible host species and more BTV serotypes. However, control of BT can be achieved by protecting the susceptible animals from vector *Culicoides* but always this is also not possible. Control of vector can be done by using insecticides, but it is expensive and does not provide complete relief from the vector. In India, modified live vaccines (MLVs) are not preferred due to nomadic nature of animals' results in spreading of the disease. Therefore, for management and control of BT, inactivated multivalent vaccines are preferred (Chand et al., 2015).

2.4 Sheeppox and goatpox

Sheeppox virus (SPPV) and goatpox virus (GTPV) belongs to a member of the genus *Capripoxvirus* of the family *Poxviridae*. The sheeppox and goatpox diseases are notifiable to Office Internationale des Epizooties (OIE) due to its economic impact. In India, sheeppox and goatpox diseases are endemic, which are host specific and pose a serious economic loss to small ruminant husbandry (Bhanuprakash et al., 2006; Bhanuprakash et al., 2010; Bhanuprakash et al., 2011). Although, SPPV and GTPV are considered as host-specific they can cross the species barrier i.e. these viruses can infect both species (Santhamani et al., 2015). The outbreak of capripox was first reported in 1936 in India, and since then, frequent outbreaks have been reported throughout the country in almost all the states where sheep and goats are reared. The occurrence of the disease is usually observed throughout the year, however, most frequently seen during the rainy season (Garner et al., 2000). Mortality in young animals can exceed 50%. A recent report revealed that the morbidity and mortality rates in the flock were 18.4% and 6.3%, respectively (Hemadri & Hiremath, 2011). Exotic and young animals are highly susceptible (Bhanuprakash et al., 2006). Certain predisposing factor for spreading out the disease is the presence of a virus on the wool of the recovered animal. The virus can be transmitted by aerosols from diseased animals, through direct contact with abraded skin and mucosa or indirectly by vectors through mechanical transmission (Kitching & Mellor, 1986).

Direct losses due to mortality are low, however, morbidity and post-disease impacts on leather quality, wool, and meat productivity are more (Bhanuprakash et al., 2011). In the Maharashtra state of India, the economic losses due to capripox diseases are calculated as Rs. 105 million (US\$2.3 million) with an average morbidity and mortality of 63.5% and 49.5%, respectively, and after 6 years the flock recovered from outbreak (Garner et al., 2000). By the estimation of these losses, the predicted total annual loss is Rs. 1250 million (US\$ 27.47 million) at the national level (Bhanot et al., 2009). The recovered animals from infection shall acquire lifelong immunity. In India, the slaughter policy and movement restrictions for disease control are difficult to follow due to various socio-economic factors. Therefore, an economical and sustainable approach for disease control is mass vaccination. Recently, P32-gene based PCR-RFLP and RPO30 and GPCR genes based sequencing analyses have been applied for the differentiation of Indian strains of SPPV and GTPV from field

samples (Santhamani et al., 2013; Santhamani et al., 2014; Santhamani et al., 2015). Vaccination is practiced for many years mainly for sheep pox to decrease the endemic nature of the disease. Recently, live goat pox vaccine has been developed to reduce the disease incidence in goats (Bhanuprakash et al., 2011).

2.5 Infectious Bovine Rhinotracheitis (IBR)

Bovine herpesvirus 1 (BoHV-1) causes IBR, which consist of various clinical manifestations such as pustular vulvovaginitis, rhinotracheitis, balanoposthitis, infertility, abortion, mastitis, conjunctivitis and encephalitis in cattle. Mehrotra et al. (1976) first reported the disease in Uttar Pradesh, India and isolated the virus from calves affected with keratoconjunctivitis. Afterwards, the disease was reported from various parts of the country in India. The disease prevalence was more in crossbred and exotic breeds of cattle when compared to local breeds of cattle (Majumder et al., 2015a). IBR is usually transmitted by semen posing a serious risk to productivity and reproductive health (Huck et al., 1971). BoHV-1 is considered as most commonly found viral agent in the semen of bovines. Akin to other herpes viruses, BoHV-1 can cause latent infection and animals turn into reservoirs of the virus in the herd. Reactivation of virus from latent infection leads to shedding of the virus in the bull semen. BoHV-1 is maintained in the environment due its short cycle of infection, latent infection, resistance to environmental factors and reactivation during stress conditions (Muykens et al., 2007; Nandi et al., 2009). BoHV-1 can cause considerable economic losses due to loss of body condition, abortion, milk yield, temporary failure of conception, loss of newborn calves, insufficient feed conversion, secondary bacterial pneumonia, cost of treatment and impact on national and international trade on germplasm and livestock (Gibbs, 1981; Majumder et al., 2015a). The mortality and morbidity rates differs among the breeds of cattle, which was lesser in milch breeds of cattle viz., 3% mortality and 8% morbidity when compared to beef breeds and feed lot cattle, which shows higher mortality rates of 20-30% (Barenfus et al., 1963). The disease is not sex dependent as male and females are equally susceptible. Crossbred cattle are more susceptible than indigenous breed (Krishnamoorthy et al., 2015). Field virus infection or immunization using an avirulent strain of BoHV-1 virus resulted in development of latent infection. Sero-epidemiological data of BoHV-1 during 2009-10 in cattle and buffalo showed that the prevalence of disease was more in Tamilnadu (67% prevalence rate) and Meghalaya state is being lowest in prevalence (Selvaraj et al., 2008). The significant levels of antibodies were detected in bovines having a history of reproductive problems and abortions. A study revealed high antibody prevalence of BoHV-1 in cattle (50.9%) and buffaloes (52.5%) from India (Renukaradhy et al., 1996).

The disease was reported in the yak with the overall prevalence of 40.8% (Rahman et al., 2007) and Mithun with overall prevalence of 19% (Rajkhowa et al., 2004). In general in India, the prevalence rate of disease was 34% with differing

prevalence rates in various parts of the nation includes 39% north-eastern, 37% northern, 25% central, 24% western and 17% eastern (Selvaraj et al., 2008; Bandyopadhyay et al., 2009a; Sarmah et al., 2015). In a recent report, 18% seropositivity was reported in bovine serum samples in Tripura (Majumder et al., 2013a). The BoHV-1 can be detected by virus isolation, SNT, FAT in infected tissues, ELISA, and IPT. Virus isolation using cell culture has been commonly practised (Majumder et al., 2015a). There are very limited information is available on molecular characterization of Indian BoHV1. Very recently, gB, gC, and gD genes of Indian BoHV-1 isolate were characterized (Majumder et al., 2013b; Majumder et al., 2014, Majumder et al., 2015b). The increased percent prevalence of the disease in recent past indicates that the problem should be tackled by adopting strict sanitary measures, maintaining 2-3 weeks of quarantine period before introducing new stock to the herd and segregation of virus positive animals, vaccination and use of semen from disease free animals. In order to get rid of the virus from a herd, identification and slaughtering of infected animals are required due to the possibility of reactivation of virus from latent infection (Majumder et al., 2015a).

2.6 Bovine viral diarrhoea (BVD)

BVD is an endemic disease worldwide and causes considerable economic losses in cattle farming community. It is caused by bovine viral diarrhoea virus (BVDV) belongs to the genus *Pestivirus* of the family *Flaviviridae*. Based on the pathogenic behaviour in cultured cells, cytopathic and non-cytopathic biotypes of BVDV are identified. BVDV consists of two genotypes (type 1 and 2) and further subdivided into several genetic and antigenic variants. Both the genotypes cause acute and persistent infection. Although the main focus of the research in cattle, the virus can infect wider range of species including domestic and mountain goats (Nelson et al., 2015). The economic losses are due to prenatal infections, infertility, abortions, congenital anomalies in calves, more neonatal deaths and persistently infected (PI) calves, which die due to mucosal disease. The incidence of BVD is usually unnoticed due to 70 to 90% of infections were in subclinical form (Neibergs et al., 2011). The BVDV was isolated from clinical samples for the first time in India by Mishra et al. (2004). The incidence of BVD in cattle (Sood et al., 2007), sheep and goats (Mishra et al., 2009) and buffaloes (Mishra et al., 2008) in India has been reported using molecular confirmatory tools. Commonly circulating genotype in BVDV in Indian cattle is BVDV-1b (Mishra et al., 2004). BVDV-2 was identified from sheep and goats (Mishra et al., 2007; Mishra et al., 2008) and cattle (Behera et al., 2011) might be due to unrestricted migration and trading in ruminants.

Various serological studies have indicated the prevalence of BVDV antibodies in Indian cattle population (Nayak et al., 1982; Mukherjee et al., 1989; Sudharsana et al., 1999; Mishra et al., 2011). Post infected (PI) animals maintain the virus and play a major role in the spread of the virus among cattle population (Broderson, 2014). PI animals acquire the infection

by in utero from non-cytopathic biotype of BVD virus during 45 to 125 gestation period results in immunotolerance (Hessman et al., 2012). PI animals excrete more viruses throughout their lifespan and act as a major source of virus spread between and within the farms. Because PI animals give negative results for a serological test for antibody detection, however, positive for BVD antigen, hence assays targeting viral antigens detection are ideal for their diagnosis in a herd.

2.7 Picobirnaviruses

The picobirnaviruses (PBV) have been identified as the emerging pathogens associated with enteric and respiratory infections in a number of mammalian and avian species. These are small structured viruses of nearly 35 nm with double-stranded bisegmented RNA genome. PBVs have been designated as genogroup I (GGI), genogroup II (GGII) and genogroup III (GGIII) based on sequence analysis of genome segment 2. In India, PBV was for the first time detected in bovine in West Bengal in 2009 (Ghosh et al., 2009) and subsequently from central India (Malik et al., 2011b). A PBV strain isolated from western Maharashtra from a buffalo calf showed huge genetic divergence (Malik et al., 2013a). Recently, we have identified and characterized a novel genogroup II picobirnavirus from a cattle calf (Malik et al., 2014), which is the first report of genogroup II detection from bovines. PBVs are detected together with other major enteric viruses such as rotavirus, astrovirus, coronavirus etc and are gaining importance these days. It is presumed that PBVs could be a potential threat for growing livestock industry due to leading gastroenteritis and associated economic issues.

2.8 Bovine rotaviruses

Rotavirus (RV) leads to severe gastroenteritis and has become a major health problem throughout the world. The RV infections enforce colossal economic losses mainly due to increased morbidity and mortality, treatment and poor growth performance of enteritis-affected animals. Though considerable research has been carried out on RV disease in humans in India, information is scanty on animal rotaviruses epidemiology. The RV associated clinical signs may vary from asymptomatic/subclinical to severe enteritis. The RV prevalence has been reported between 3.25% to 42% using serological and molecular methods during 1990-2001 (Mittal et al., 1991; Shah & Jhala, 1992; Agarwal & Singh, 1993; Gulati et al., 1995; Jindal et al., 2000; Khurana & Pandey, 2001). The information generated through VP7 gene (G) and VP4 gene (P) genotyping of bovine RVs in various epidemiologic surveys confirms that (i) G3, G6, G8 and G10 constitute more commonly circulating G genotypes and P[11] as the P genotype in the country; (ii) other G types, such as G15 with P[15] and P[21] types have been detected but are localized in some parts of the country; (iii) multiple G and P types can co-circulate within the same region (Malik et al., 2012) and can cross the inter-geographical boundaries of the states (Malik et al., 2013b). Concurrent infection with two or more pathogens is a common phenomenon and interactions among multiple

pathogens often appear to generate a more severe or chronic outcome than is observed with the individual pathogen (Minakshi et al., 2009). Still very little is known about the specific interactions which occur in concurrent infections. Minakshi et al. (2009) reported the occurrence of dual infection of bovine group A rotavirus in a diarrhoeic calf in one of the northern state, Haryana, India. Malik et al. (2012) described the detection of G3 genotype in combination with G8 or G10 genotype. The control of the virus infection in both humans and animals is dependent on regular monitoring of newly emerging RVs and production of an effective vaccine to control rotavirus associated enteritis in young calves remains a challenge throughout the world.

3 Bacterial diseases of ruminants

3.1 Haemorrhagic septicaemia (HS)

Haemorrhagic septicaemia (HS) is the most significant bacterial contagious infection in cattle and buffaloes with proven endemicity in India (Shivachandra et al., 2011). The disease usually causes devastating and alarming problem in buffaloes and cattle. The course of disease becomes fatal when the aetiological agent enters in non-endemic areas of reared bovines. The disease was more severe in buffaloes when compared to cattle and young and young adult animals manifest more severe form of disease than older animals (Singh et al., 2014a). Moreover, the disease is widely reported from bison, African buffalo, camels, elephants, horses, donkeys as well as from yak. HS is an acute, fatal and septicemic disease of cattle and buffaloes caused by *Pasteurella multocida* (Rajeev et al., 2011; Shivachandra et al., 2011). *P. multocida* causes HS in cattle and buffaloes, and pneumonic pasteurellosis in sheep and goats. The most prevalent serotypes in India are B:2, A:1, A:1,3, A:3, A:4, A:3,4,12, F:3, D:1, D:3, F:1, F:4 and F:4, 12. In an Indian molecular study of MLST conducted by Sarangi et al. (2016), 10 different sequence type were identified as ST 122, ST 50, ST 9, ST 229, ST 71, ST 277, ST 129, ST 280, ST 281 and ST 282. The B:2 serotype in India in pigs causes sporadic septicaemic disease. Apart from buffaloes, sporadic occurrence of the disease with 62% outbreak rates in goats, 102% in sheep and 5% in pigs has been reported during 2007-2010. An estimated economic loss due to haemorrhagic septicaemia in India is Rs. 225 million per year (Singh et al., 2008a).

The economic loss due to HS has been calculated as Rs. 6816 per infected cattle and Rs. 10901 per infected buffalo. The total economic loss was Rs. 5255 crore estimated from throughout India. Among that, about 80.3% economic losses are due to direct effects of HS and 19.7% economic losses are due to indirect effects of HS. In HS, about 74.8% of the economic losses are due to affections in calves and 25.2% are due to losses in adults (Singh et al., 2014a). In India, HS is the leading cause of mortality and second most commonly encountered disease during 1991 to 2010 reported by National Animal Diseases Referral Expert System (NADRES). According to NADRES report, approximately 97% of the HS

outbreaks were occurred in cattle and buffaloes (Gajendragad & Uma, 2012). Epidemiological data of HS obtained during 1974 to 1986 revealed that it was the leading cause of mortality and second leading cause of morbidity than other enzootic diseases like RP, FMD, BQ and anthrax (Dutta et al., 1990).

During the last 4 decades, it has been found that HS caused 46 to 55% of mortality in bovines in India (Benkirane & De Alwis, 2002). Diagnosis can be made on the basis of clinical signs and post-mortem findings and confirmatory diagnosis can be done by isolation and identification of etiological agent with appropriate staining (Rajeev et al., 2011). Vaccination is a major tool for the control of disease especially 2 to 3 months before the high-risk monsoon season. Although various HS vaccine types like oil adjuvant, alum-precipitated and various emulsion vaccines are commercially available, the search for suitable vaccines with long-lasting immunity and the good protective response is required. Good sanitary measures, early diagnosis, quarantine, isolation of infected animals, immediate antibiotics treatment, deep burial or incineration of carcasses and restriction of animal movements to disease-free areas are essential.

Awareness of the disease among farmers is required for effective disease reporting system (Benkirane & De Alwis, 2002; Shivachandra et al., 2011). *P. multocida* has a zoonotic potential and infection to human spread through bites and scratches of the animals (especially dogs and cats) (Aski & Tabatabaei, 2016). The infection may lead to ocular infection to fatality in humans (Corchia et al., 2015; Talley et al., 2016). Shivachandra et al. (2013) studied the genetic relatedness of *ptfA* gene among *P. multocida* isolates of different species and observed that avian isolates are divergent from mammalian isolates (Shivachandra et al., 2013). Recombinant Omp87 protein of *P. multocida* serogroup B:2 strain P52 elicited increase in IgG response and provided a different level of protection against homologous and heterologous challenge (Kumar et al., 2013). Similarly, rVacJ protein elicited antigen-specific IgG response in immunized mice (Shivachandra et al., 2014b) and comparative amino acid sequence of different *P. multocida* isolates showed absolute homogeneity (Shivachandra et al., 2014a). In another study, it was demonstrated that recombinant transferrin binding protein A (rTbpA) elicited I antigen specific IgG response and provided a different level of protection in mice challenge (Shivachandra et al., 2015).

3.2 Black quarter (BQ)

BQ is a highly fatal and acute bacterial infection of cattle caused by *Clostridium chauvoei* affecting buffaloes, sheep, and goats. Young cattle and buffaloes with 6 to 24 months of age and good body condition are highly susceptible. *C. chauvoei* is normally present in the intestine of animals. In the soil, spores remain viable for many years and can act as a source of infection to animals. BQ is a soil-borne infection and outbreaks occur most commonly during the rainy season, in areas with moderate rainfall, where dry-crop cultivation is commonly

practised. This disease is widely prevalent in cattle belonging to Karnataka, Andhra Pradesh, Tamil Nadu and Maharashtra states of India. One sporadic outbreak of the disease from eight HF crossbred cows has also been reported by Zahid et al. (2012) from Ludhiana, Punjab. During 2009-10, the highest outbreak of disease were reported from West Bengal with 95 outbreaks, in which 293 animals were affected and 122 animals were died and then in Maharashtra with 37 outbreaks, in which 128 animals were affected and 96 animals were died (Hemadri & Hiremath, 2011). Combined prophylactic vaccine consists of aluminium hydroxide adsorbed and formalin inactivated cultures of *C. chauvoei* and *P. multocida* gives protective immunity against BQ and HS. Prior to operation in ruminants, proper disinfection of surgical instruments is necessary to avoid infection.

3.3 Anthrax

Anthrax is a highly fatal, acute and febrile zoonotic disease. It is enlisted in top five diseases of zoonotic importance in India where attention has to be prioritizing (Sekar et al., 2011). Cattle and sheep are highly susceptible to anthrax followed by horse, mules and pig. It is a soil-borne infection, caused by *Bacillus anthracis* and outbreaks generally occur after the climatic change. The disease is endemic in south Asia and Bangladesh (Thapa et al., 2014), especially enzootic in India and endemic in Karnataka, Tamil Nadu, Andhra Pradesh, West Bengal, Orissa, Maharashtra and Jammu and Kashmir (Gunaseelan et al., 2011). The "incubator zones" for the presence of anthrax is an alkaline soil pH and dry periods which provides the microenvironment for spore survival and increased exposure to susceptible hosts. Majority of the disease incidence were encountered in cattle followed by sheep or goat, buffalo, pig and elephant in India. Although the disease is restricted to herbivores, but few sporadic cases from wildlife captive animals like hyena of Nandanvan zoo, Chattisgarh have also been reported in recent past (Patil, 2010). The possible role of the insects like house fly (*Musca domestica*) in spreading the disease among animals also cannot be ruled out (Fasanella et al., 2010). Beside that another important source of spread of infection is a bone meal which is an essential additive of animal feed as well as in fertilizers; being frequently imported or exported among developing countries (Davies & Harvey, 1972). The epidemiological data collected during 2002-2010 from bovine outbreaks of anthrax, showed maximum outbreaks of disease in West Bengal, in which 631 animals were affected with disease and 564 animals were died. In small ruminants especially sheep, the highest outbreaks of disease were encountered from Andhra Pradesh and Karnataka which might be due to more sheep population in these states and also unresstricted migratory patterns. The important tools for the prevention of anthrax are vaccination, avoiding opening of the carcass, proper carcass disposal, burning of the bush, appropriate treatment, and in order to avert a future outbreak, annual revaccination is necessary for the outbreak area for at least three years (Chelsea et al., 2008).

3.4 Enterotoxemia (ET)

Enterotoxemia (ET) is a severe disease of ruminants caused by *C. perfringens* types B, C and D with more case fatality rates results in considerable economic losses to the farmers (Rood & Cole, 1991). ET is otherwise called as pulpy kidney or overeating disease. The disease affects cattle, sheep, and goats. Sheep and goats of all the age group are affected however younger animals are more prone to infection. The bacteria are usually present in fewer numbers in the intestine of sheep and goats. Where there is sudden change either in food or in the environment, the disease precipitates. Overgrowth of the *C. perfringens* occurs due to excessive consumption of milk or large amounts of grain, immunosuppression, heavy gastrointestinal parasitism, ration rich in carbohydrates and low in roughage, and reduced gastrointestinal motility.

In India, during the commencement of monsoon season, frequent disease outbreaks of enterotoxaemia in sheep were encountered every year, in spite of frequent vaccinations against *C. perfringens* Type D (Kumar et al., 2014). Severe enteritis and sudden death in lambs are caused by type B and C infections. Kumar et al. (2014) reported the prevalence of *C. perfringens* type C for the first time in India. Major causative agent for enterotoxemia is *C. perfringens* type D and *C. perfringens* type B and D produces epsilon toxin, which is responsible for lethal ET (Arya & Bhatia, 1992). Epsilon toxin is initially secreted as inactive prototoxin, which undergoes trypsin digestion leads to conversion of active toxin by losing N-terminal peptide (Bhown & Habeeb, 1977).

The mature epsilon toxin is responsible for highly lethal, dermo necrotic and edematous activities. The clinical signs in sheep are colic, diarrhoea and neurological symptoms. Post-mortem lesions are widespread vascular congestion, with cerebral, cardiac, pulmonary, and renal oedema (Uzal et al., 2004). A sporadic case of the disease outbreak has also been reported in camel calf with the association of *C. perfringens* type A. During 2006, highest number of outbreak was encountered in India. Majority of the disease outbreaks were recorded from AP, Tamil Nadu, Karnataka, Maharashtra and Jammu and Kashmir. An estimated 12,929 sheep and 619 goats have died due to ET since 2002 (http://www.icar.org.in/files/Vision%202030_PDADMAS-11-01-2012.pdf). In the recent past, the number of disease outbreaks became reduced significantly due to the efficient vaccination strategies. The animals affected with disease should not be vaccinated, because it will flare up the disease outbreak. The vaccination strategy for young animals includes primary dose at 4 weeks of age and booster revaccination at 1 month later of primary dose and all the adult animals should be vaccinated yearly once. Recently, an inactivated whole-cell vaccine was developed and commercialised for the control and eradication of ET, however major disadvantage of this vaccine is local reactions at the site of inoculation. Recently, for sheep combined aluminum hydroxide adjuvanted epsilon toxoid (recombinant) and live attenuated freeze-dried sheep pox vaccine is developed (Chandran et al., 2010).

3.5 Brucellosis

Brucellosis is one of the five main notifiable bacterial diseases of zoonotic importance in the world. Brucellosis is a disease of animals with humans as an accidental host (Joshi & Parkash, 1971). *Brucella* is a Gram-negative facultative intracellular bacteria and bovine brucellosis is caused by *B. abortus*, less frequently by *B. melitensis* and rarely by *B. suis*. Cattle and buffaloes harbor predominantly *B. abortus* biotype-1; followed by biotype-3; rarely biotypes-2, 4, 5, 6 and 9 (Renukardhya et al., 2002). Out of 6 *Brucella* spp., *B. melitensis*, *B. abortus*, *B. suis* and *B. canis* can cause infection and clinical symptoms in man in the descending order of pathogenicity (Smits & Kadri, 2005). The disease has been eradicated from the livestock populations of most European countries, Japan, Canada and the USA. The disease is highly endemic in different states of the country and reported in different animal species like cattle, buffalo, sheep, goats, camel, yak and pig (Smits & Kadri, 2005). But, the highest prevalence is seen in dairy cattle. There are various reasons of its endemicity viz. ignorance of carrier animals, ineffective test and slaughter policy in most of the Indian states, improper and unplanned vaccination, no effective quarantine and uncontrolled trans-state migration of animals (Renukardhya et al., 2002). By seeing the intensification of disease in recent past, it seeks to review the ongoing policies implemented for its eradication and/ or control. Bovine brucellosis is now have been eradicated from many countries but as it is still prevailing in many states of our country; we are lagging behind in various ruminants' production like milk and meat etc. (Singh et al., 2015a).

In India, brucellosis was first recognized in 1887 and since then the cases are being observed in almost all the states of the country. In India, on an average, the disease causes revenue losses of INR 420 per cattle, INR 1100 per buffalo, INR 42 per sheep, INR 30 per goat and INR 36 per pig with the total economic loss of Rs. 350 million. It is also reported from the Yak (Renukardhya et al., 2002; Bandyopadhyay et al., 2009b; Singh et al., 2015a). Higher prevalence of disease was reported from goats in Bihar and Madhya Pradesh states and in sheep Rajasthan and Karnataka states of India. The overall prevalence of disease was 8.85% in goats and 6.23% in sheep in India (Joshi et al., 1975; Chatterjee et al., 1986; Suresh et al., 1993; Gill et al., 2000; Renukardhya et al., 2002; Hemadri & Hiremath, 2011). In spite of significant improvements made in diagnosis and therapeutic advances, brucellosis emerged as a widespread and highly prevalent disease in many developing countries. The sero-epidemiological data collected during 1994 to 2001 from various states of India revealed that the disease in cattle and buffalo was more prevalent in Union Territory of Delhi followed by Andaman and Nicobar islands, West Bengal, Tamilnadu, Kerala, Gujarat, Maharashtra and Punjab. The annual sero-prevalence data reveals increasing trend of the disease in India. The representative samples collected from different states of the country showed that the prevalence rate become increased from 34.15% during 2006-07 to 67.28% during 2010-11 (Gill et al., 2000; Renukardhya et al., 2002; Hemadri & Hiremath, 2011). Control and management of

animal brucellosis include careful herd management, hygiene, and vaccination. Many countries attained brucella free status by employing test and slaughter policy. However, in India, only “test and segregation” policy is practically adaptable to control the disease in conjunction with efficient preventive measures and control of animal movements. Vaccination is the practical, feasible and effective approach for the control of brucellosis in our country. Hygienic disposal of uterine discharges, foetus, foetal membranes is required. Increased public awareness through health education programmes is necessary. Vaccination with *B. abortus* strain 19 vaccine (Bruvax; Indian Immunologicals Limited, Hyderabad) is in use for female cattle and buffalo calves between 4 to 6 months of age followed by annual revaccination and all adult females just after parturition. The advantages of calf hood vaccination are the prevention of abortions in the herd produces short-lived antibody response up to 6 to 8 months after vaccination, no booster vaccination required and builds herd immunity in 3-5 years period. The vaccine should not be administered to pregnant animals, bulls and male calves (Kulshreshtha et al., 1978; Renukardhya et al., 2002; Hemadri & Hiremath, 2011; Shome et al., 2012).

3.6 Leptospirosis

Leptospirosis is a re-emerging zoonotic disease in Asia especially in India, Africa and Latin America and widespread in those countries having a hot and humid temperature. Till date, 210 pathogenic *Leptospira* serovars have been identified which have been placed into 24 serogroups based on antigenic similarity. The genus *Leptospira* consists of 2 species known as *L. interrogans* and *L. biflexa*. The pathogenic species are *L. interrogans*, *L. borgpetersenii*, *L. inadai*, *L. meyeri*, *L. noguchii*, *L. santarosai*, *L. weilli*, *L. wolbachii*, *L. fainei*, *L. alexanderi*, *L. parva* and *L. kirschneri*. *L. biflexa* is the saprophytic species. Most commonly reported serovars responsible for the infection in man and animals are Autumnalis, Icterohaemorrhagiae, Canicola, Pomona, Grippotyphosa, Hebdomadis, Australis, and Hardjo. These serovars have been also commonly reported from wild animals and natural carriers such as rodents (Srivastava, 2008; Himani et al., 2013). The disease leptospirosis was first reported in 1988 as Andaman haemorrhagic fever. It has attained significant consideration in recent past as the incidences are being increased among various livestock species in India. Leptospirosis is endemic in India, from 20th century onwards and many outbreaks of disease have been encountered in coastal regions of West Bengal, Maharashtra, Gujarat, Tamil Nadu, Kerala, Orissa, Karnataka and Andaman and Nicobar Islands (Varma et al., 2001). Majority of the disease incidences are happening between October to November which correlates with the monsoon season. The disease was initially reported from Indian cattle by Adinarayanan et al. (1960). Subsequently, several other workers also reported its incidence and prevalence (Srivastava et al., 1991; Varma et al., 2001; Sivaseelan et al., 2003).

The disease is of significant economic importance in terms of losing livestock through abortions and increasing treatment cost for repeat breeding cases. The disease mostly precipitates with the monsoon season. The reservoir for the etiological agent is rodents in principal along with cattle, pig, and dog. Sero-epidemiological data of leptospirosis conducted during 1995 from different states of India revealed that highest prevalence in dogs (15.9%) followed by horses (14.6%), sheep (12.5%), cattle (7.5%) and buffaloes (5.4%) (Srivastava et al., 1991; Sivaseelan et al., 2003; Srivastava, 2008). During 2007 outbreak in Karnataka, a total of 1,516 cases and southern parts of Gujarat in 2011, 130 deaths within a span of two months were reported (<http://www.gideononline.com>; Promed, 2011). Recently, 209 cases of disease with 12 cases of deaths in Kochi and Kerala, and 16 deaths from districts of Surat and Valsad of Gujarat were recorded in October 2012 (<http://www.healthmap.org>). A seroprevalence rate of 71.12% was reported from Kerala where highly prevalent serovar is *Leptospira interrogans* serovar Autumnalis followed by Australis, Pomona, Canicola, Pyrogenes, Icterohaemorrhagiae, Javanica and Patoc (Ambily et al., 2013). These alarming reports highlight the constant risk of leptospirosis and emergence of new serovars other than the vaccine serovars demands the inclusion of these serovars in the vaccines due to serovar-specific immunity in leptospirosis (Sambasiva et al., 2003).

Since leptospires are fastidious and slow growing organisms, isolation of organism is difficult due to 6 weeks required for organisms to grow. Most widely used test for diagnosis of leptospirosis is microscopic agglutination test (MAT) and a titre of 1:100 or more indicates infection in seroprevalence studies (Srivastava, 2008; Himani et al., 2013). The prevention and control of leptospirosis in domestic animals and man are difficult to achieve due to the widespread distribution of leptospires in wildlife and long-term carriers. The diseased animals should be immediately isolated for at least 2 weeks and the premises should be thoroughly disinfected. The carrier animals shedding the organisms in the urine should preferably be slaughtered and buried or burnt.

Since leptospirosis is an occupational hazard all the persons directly involved with animals or its environment should use gumboots, gloves, aprons etc. Rodent control using rodenticides, better hygienic practices and environmental hygienic measures to avoid the risk of water, soil and food contamination are necessary to check the transmission of leptospirosis (Sambasiva et al., 2003; Srivastava, 2008; Himani et al., 2013; Patil et al., 2014). Although in wild animals vaccination is not possible, and in domestic animals vaccination strategy can be applied for control and prevention of leptospirosis using outer membranes of bacteria and/or whole cell inactivated with chemical agents (Palaniappan et al., 2002).

3.7 Listeriosis

Listeriosis also known as circling disease, silage disease and meningoencephalitis, and a fatal disease of ruminants like sheep, goat, cattle, buffalo, camel, and non-ruminants like horse, pig, canine, rodent, wild animals, birds and also humans (Malik et al., 2002; Barbuddhe et al., 2012; Dhama et al., 2013a, 2015a). Among small ruminants sheep are mostly susceptible. Recently, listeriosis caused 23,150 illnesses, 5463 deaths and 172,823 disability-adjusted-life-years worldwide (De Noordhout et al., 2014). It is an important foodborne zoonotic disease caused by intracellular pathogen *Listeria monocytogenes*, which does cell to cell entry results in the crossing of blood-brain, intestinal and placental barrier (Hernandez-Milian & Payeras-Cifre, 2014; Dhama et al., 2015a). The organism can survive at various temperatures ranges from 4 to 37 °C (Janakiraman, 2008). The organism has several virulence factors like internalins, hemolysin, metalloprotease, listeriolysin-O (LLO), fibronectin-binding protein-A (FbpA), phospholipases and bile exclusion system which are necessary for intracellular multiplication, adhesion and pathogenesis (Vera et al., 2013). The disease occurs as sporadic or epidemic form throughout the world; however during an outbreak, it causes severe damage (Dhama et al., 2015a). Mostly the disease in animals occurs as subclinical but severe forms can also occur. The clinical manifestations of listeriosis include septicaemia, meningoencephalitis, abortion with placentitis in last trimester, stillbirth, perinatal infections and gastroenteritis (Janakiraman, 2008; Barbuddhe et al., 2012; Limmahakhun & Chayakulkeeree, 2013; Dhama et al., 2015a).

Listeriosis has unique seasonal occurrence during December to May in northern hemispheres due to the seasonal feeding of silage. More cases of abortions in sheep occurs during February and March due to late pregnancies. In humans, mortality due to listeriosis varies from 20- 30% (Barbuddhe et al., 2012; Dhama et al., 2013a, 2015a). Listeriosis can be transmitted by ingestion of feed and water contaminated with saliva, nasal secretions, faeces and aborted materials from infected animals and also inhalation of dust and soil contaminated with bacteria (Brugere-Picoux, 2008). Ready-to-eat foods and animal origin foods like milk, meat, and their products play a crucial role in the transmission of listeriosis to humans (Rebagliati et al., 2009). Young lambs (under 5 weeks of age) will suffer from septicemic form while the encephalitic form is noticed in older lambs (4-8 months). It causes abortion and stillbirth in pregnant women and in fetuses it causes abscesses and granulomas in various organs like lungs, liver, and spleen (Drevets & Bronze, 2008). In India, genital listeriosis is very common and correct epidemiological data are not available due to under-reporting and poor diagnostic facilities (Malik et al., 2002). Studies regarding the prevalence of Listeriosis in various developing countries are necessary to identify the accurate status of disease throughout the world (De Noordhout et al., 2014). Treatment of listeriosis is a difficult task due to the invasion of all cell types. Drugs of choice for listeriosis are erythromycin and ampicillin. Control of listeriosis is difficult due to ubiquitous nature of bacteria in the

environment, lack of a simple method for identification of *Listeria* and poor understanding of risk factors except silage (Malik et al., 2002). Good management practices like proper disposal of contaminated materials, beddings and litters, and infected carcasses should be done carefully by incineration or burning methods. Consumption of unpasteurized milk or uncooked meat should be avoided (Rebagliati et al., 2009).

3.8 Tuberculosis

Bovine tuberculosis (bTB) is a chronic bacterial zoonotic disease and easily spreads to humans through inhalation of aerosols or ingestion of unpasteurized infected milk (Prasad et al., 2005). Tuberculosis is caused *Mycobacterium tuberculosis* complex (MTC) belongs to the genus *Mycobacterium*. MTC has four species namely, *M. tuberculosis*, *M. bovis*, *M. africanum* and *M. microti*. *M. tuberculosis* mainly affects humans, whereas *M. bovis* causes bovine tuberculosis and affects wide host range including domestic as well as wild animals (Grange, 2001; Verma et al., 2014a). The bTB is widely prevalent and causes 10-25% loss in productivity (Verma et al., 2014b). In developing countries, there is increased the incidence of *M. bovis* infection in humans causing serious public health problem due to sharing of the same habitat in domesticated animals and humans (Grange, 2001). In Africa, bTB endemic zones nearly 85% of cattle and 82% of the human populations were living together (Michel, 2002). Organisms are excreted in exhaled air, sputum, faeces, urine, milk, vaginal and uterine discharges, and discharges from open peripheral lymph nodes (Verma et al., 2014a). There are limited reports available from India and many epidemiological and public health aspects of the infection remain largely unknown (Neeraja et al., 2014a; Neeraja et al., 2014b; Baqir et al., 2014; Verma et al., 2014b). An overall prevalence of bTB in India is 14.31 to 34.42% (Thakur et al., 2010). *M. bovis* mainly causes extra-pulmonary forms of tuberculosis and major route of transmission is the oral route. Bovine tuberculosis has been classified as list B disease by OIE due to various socio-economic and public health concerns at the national level as well as the international trade of livestock and their products.

Various wild animals like badgers, brushtail possums, deer, bison and African buffalo play an important role in the maintenance of *M. bovis* infection in wildlife communities and the spread to domestic animals. The test and slaughter policy is effective for tuberculosis control, however in India difficult to follow due to various social and economic constraints and the existence of more wildlife reservoir. In the early stage of infection, test and segregation are recommended while in the terminal stage of infection, test and slaughter is followed. Hence, it is difficult to eradicate bTB infection from livestock until transmission between wildlife and domestic animals has prevented. Better diagnostic tests for rapid screening of disease at the field level should be developed (Sandhu, 2011). The main diagnostic test used for screening of bovine tuberculosis is the tuberculin test (Baqir et al., 2014; Neeraja et al., 2014a; Neeraja et al., 2014b). For control of bTB in India requires

vaccination in livestock and captive wildlife species with collaborative efforts between agriculture, wildlife, environmental and political authorities. Pasteurization of milk before marketing and organized abattoirs with carcasses can be routinely tested for TB (Sandhu, 2011). Bacillus of Calmette and Guérin (BCG) vaccine is used for TB, which is a live, laboratory-attenuated strain of *M. bovis* (Waters et al., 2014).

3.9 Paratuberculosis (or) Johne's disease

Paratuberculosis also known as Johne's disease (JD) is infectious, chronic granulomatous enteritis of cattle and buffaloes caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP) (Singh et al., 2014b). JD is a deadly, emaciating and chronic wasting disease characterized by weight loss and profuse diarrhoea. JD mainly affects domestic and wild ruminants and poses serious economic loss to the dairy industry. JD is endemic in farms throughout the country. Most of the time, the disease unnoticed due to chronic nature of the disease and unfamiliar symptoms to the clinicians and farmers (Tripathi, 2008). It is a zoonotic disease and causes Crohn's disease (CD) in humans (Greenstein, 2003). High prevalence of MAP antibodies (Indian bison type) was recorded from animal attendants having gastrointestinal problems, who were worked in endemic JD infected goat flocks in India (Singh et al., 2008b). CD is a non-specific chronic inflammatory condition of the gastrointestinal tract and clinical signs are reduced appetite, bloody diarrhoea, abdominal pain, vomiting, tiredness and weight loss. JD is a list B of OIE listed disease and animals require certification due to trade restrictions. It is calculated that almost 40% of US dairy herds are infected with JD and economic losses exceed 1.5 billion/year in dairy industry (Wells & Wagner, 2000). Animals are often infected during early life by faecal oral route. The *Mycobacterium* infect the M cells of the follicle in intestinal epithelium and then engulfed by intestinal macrophages leads to replication and viable for several months to years and development of disease (Momotani et al., 1988; Tripathi, 2008).

The disease was first reported in cattle in Lahore of undivided India, followed by another case in 1917 from a Military Dairy Farm, Hisar. Since then, many cases have been reported throughout the country with an incidence rate of 1.78 to 1.9%. MAP infecting the animals in North India has been genotyped as Bison type (Sevilla et al., 2004; Sevilla et al., 2005). High seroprevalence of JD average 29% (29.8% in cattle and 28.6% in buffalo) has been found in domestic animals by using indigenous, sensitive and MAP-specific ELISA kits in North India. The seroprevalence of JD in Uttar Pradesh (31.9%), Punjab (23.3%), Gujarat (13.39%) and Andhra Pradesh (16.26%) has been reported (Sivakumar et al., 2005; Tripathi, 2008; Singh et al., 2011; Mohan et al., 2013). In spite of very high morbidity rates and lower productivity, economic losses in production go unnoticed in India due to chronicity. The insertion element IS900 has been regularly used to identify the MAP in clinical samples (Garg et al., 2015). Management and control of JD are difficult due to the absence of rapid and

sensitive diagnostic test for diagnosis of infected animals before clinical signs develop. Due to chronic nature of the disease, it is necessary to diagnose the infection early to decrease the production losses and to avoid the infection spread to susceptible animals and humans (Tripathi, 2008).

4 Parasitic diseases of ruminants

4.1 Fascioliasis

Fascioliasis is caused by *Fasciola gigantica* and *F. hepatica*. In India, fascioliasis is more common caused by *F. gigantica*. Fascioliasis is more common in sheep and causes high economic losses to sheep rearing farmers. The incidence rate of fascioliasis in various climatic regions like tarai, hills and plains in northern region of India was recorded as 10.79% in cattle, 13.90% in buffaloes, 2.78% in sheep and 2.35% in goats (Sharma et al., 1989; Garg et al., 2009). One of the studies conducted in Gorakhpur district showed that about 94% of the buffaloes are infected with *F. gigantica* (Singh & Agarwal, 1981). *Lymnaea acuminata* has been identified to be the intermediate host (Agarwal & Singh, 1988). Livestock of Tarai region is having the maximum incidence of fasciolosis when compared to hills and plains (Malone et al., 1998). In cattle and buffaloes, high prevalence of disease was noticed during winter months (15.57% buffaloes, 11.84% cattle) followed by summer and rainy season.

However, in sheep and goats, high prevalence of disease (2.71% goats and 4.60% sheep) was noticed during rainy season. An Abattoir studies exhibits its more prevalence in buffaloes (31.14%) when compared to sheep and goats (Garg et al., 2009; Mir et al., 2013; Swarnakar & Sanger, 2014). Further, 5.48% of *Lymnaea auricularia* snails were carrying the immature stages of *F. gigantica*. The snails present in the Tarai region causes higher incidence (7.28%) of disease when compared to snails present in plains (1.57%). During 2002, higher incidence of *Fasciola* was recorded from Orissa with a total of 545 outbreaks, in which 4993 animals were affected and 34 animals were died, followed by Haryana, Manipur, Mizoram, and Bihar. Nationwide fascioliasis collective data shows outbreaks were maximum in Orissa followed by Bihar, Mizoram, Rajasthan, Haryana, Kerala, Karnataka, Maharashtra, Tamil Nadu and Gujarat (Gupta et al., 1986; Sheikh et al., 2007; Hemadri & Hiremath, 2011).

One of the methods to control the disease is to effectively control the snail population (Kumar et al., 2009). In a present era which is more concern with the environment pollution, the researcher should exercise in the direction to identify more such products which are of plant origin as well as to ensure about its biodegradability. The experiments conducted by some workers under this direction had shown proven activity of some plants like *Alstonia scholaris*, *Thevetia peruviana*, *Euphorbia pulcherima* and *Euphorbia hirta* act as snailicide (Singh et al., 2010).

4.2 Trypanosomiasis

Trypanosoma evansi causes Trypanosomiasis, which is a significant haemoprotozoan infection of wild animals, dogs, horses, camels, donkeys, cattle and buffaloes. The outbreaks are reported in water buffaloes in India (Tewari et al., 2013; Pandey et al., 2015). The disease was originated from North Africa and through the Middle East it reaches into India (Desquesnes et al., 2013). All domestic animals except camels, the disease is commonly known as Surra and in camels the disease is known as Tibersa. *T. evansi* is the most commonly occurring trypanosome species in India and causes major economic losses in horses and camels (Tewari et al., 2013). Tabanidae flies (Horse flies and Deer flies) are the vectors responsible for the spreading of the disease. There are 244 species of this vector reported in India (Banerjee et al., 2015). In dogs, the prevalence of *T. evansi* was observed higher in Mongrel than that of other recognized breeds. The young ones below 2 years of age are more commonly affected (Prasad et al., 2015). Absence of the disease transmitting vector is the major reason for non-prevalence of other trypanosome species. Due to subclinical infection, the incidence of trypanosomiasis in cattle and buffaloes has been unnoticed in India and buffaloes may act as reservoirs (Jaiswal et al., 2015). When the animals become stress due to long transportation, hard work, overcrowding, malnutrition, inclement weather and other concurrent infections, the infection flare up and become prominent and visible infection (Rani et al., 2015). The acute form of the disease in bovine is manifested as emaciation, high fever, lachrymation, corneal opacity, reduced milk yield, nervous signs and mortality often happens within 24 hours of onset of clinical signs. Chronic Surra is characterized by weight loss with loss of reproductive performance (Radostits et al., 2007). In addition to economic losses, the disease also causes immune suppression along with huge mortality in precious animals. The disease occurs in all age groups of animals. The incidence of infection is more common during 1.5 to 2 months after rain, because more availability of rain water lodged breeding areas for disease spreading vectors (Rani et al., 2015). Highest incidence of disease was reported during 2001-02 whereas least incidence of disease was reported during 2009-10. The researcher should more focus on the development of novel chemotherapeutic agents having selective and promising therapeutic potential (Sivajothi et al., 2013). *T. evansi* can be controlled by using trypanocidal drugs, control of vectors and trypanotolerant cattle breed development (Tewari et al., 2013). Diminazene aceturate (7 mg/kg b. wt) is the prescribed drug for the treatment of trypanosomiasis in ruminants and should be administered deep intramuscularly.

4.3 Theileriosis

Bovine tropical theileriosis is an inapparent disease in large ruminants, caused by *Theileria annulata* and highly fatal diseases of indigenous cattle breeds and cross breeds due to extensive cross-breeding programmes. *T. annulata* and *T. parva* are considered to be the most pathogenic species of Theileria. The incidence rate of *T. annulata* is 14.94% by

blood smear examination whereas, 30 to 60% of seropositivity was reported in cross-bred cattle in India, except Himalayan region due to unfavourable climate for tick survival (Singh et al., 1993; Naik et al., 2010; Kohli et al., 2014; Kumar et al., 2015b). Theileriosis causes a serious economic loss due to mortality and reduced milk yield. In India, the tropical theileriosis is one of the major hurdles in genetic improvement programme of Indian taurus cattle breed. The estimated economic loss due to theileriosis is approximately 800 million US dollars (Devendra, 1995). The incidence of disease is seasonal due to availability of ticks on the host, which carries the organism, was higher during summer months like May to October. Other predisposing factors favouring the occurrence of disease are stress, harse climate, concurrent disease, transportation and vaccination. Hyalomma anatolicum anatolicum transmits *T. annulata*, which is normally present in the semi desert desert and steppe. Adult and its immature stages of three host tick were present in cattle. The adult stages of tick were more active during late spring season. The immature phase of tick usually feed on the animals, and nymphs and larvae can obtain the disease by feeding on the infected animal and transmit the disease to other animals following moulting, adults or nymphs feed on other animals. The incidence of the disease is higher during March to November because this is adult feeding season; however, the nymphs have the feeding season of July to September. The occurrence of *T. annulata* is higher during late spring and early summer season (Roy et al., 2004; Magona et al., 2011; Vahora et al., 2012; Kohli et al., 2014). The epidemiological data reveals that the highest number of outbreaks was occurred from Orissa followed by Bihar, West Bengal, Jharkhand and Haryana. In India, on nucleotide heterogeneity study, it was observed that in *T. annulata* there is a strain variability as heterogeneity varies between 0.1 to 8.6. Therefore, it is also required to go for an elaborative study on the genetic diversity of the parasite which is an overlooked area till now (George et al., 2015). The disease epidemiological data showed that the incidence of disease was low during 2008 whereas the incidence was more during 2006 (Hemadri & Hiremath, 2011).

4.4 Babesiosis

In India, babesiosis in bovines is mainly caused by *Babesia bigemina* and *Babesia bovis*. The disease is prevalent in many states of the country like U.P., Orissa, Kerala, Punjab, Arunachal Pradesh, Mizoram, Meghalaya and Assam (Ravindran et al., 2002; Wadhwa et al., 2008; Singh et al., 2009a; Sharma et al., 2013; Saravanan et al., 2013). The Babesia is transmitted to the susceptible animal by Boophilus microplus, which is the one host tick. Transovarial route is the major mode of spread within the tick. The infected female adult tick can spread the disease up to 32 generations. There are some novel serological tests like slide enzyme-linked immunosorbent assay (S-ELISA), indirect fluorescent antibody test (IFAT) and molecular test like PCR available for the detection of the disease in bovines (Singh et al., 2009a; Harkirat et al., 2013).

The disease epidemiological data showed that incidence of disease was more during 2001, whereas incidence of disease was less during 2008-09. The analysis of the epidemiological data reveals that the incidence of the disease were maximum in Orissa followed by Assam, Haryana, Jharkhand, Bihar, Madhya Pradesh, Rajasthan and Himachal Pradesh (Ananda et al., 2009; Singh et al., 2012). Different diseases of ruminants and the species affected are presented in Fig. 1.

5 Emerging Diseases

Recently, many outbreaks of emerging diseases like bovine spongiform encephalopathy (BSE), paramyxovirus infection in pigs (Nipah) and horses (Hendra), severe acute respiratory syndrome (SARS), rabies, tuberculosis, bovine corona virus, Lyme disease, Crimean-Congo hemorrhagic fever, West Nile virus and zoonotic H5N1 avian influenza were detected, which causes significant morbidity and mortality in the developing world (Hansa et al., 2013; Verma et al., 2014a; Goswami et al., 2014; Madhu et al., 2016). Many diseases re-emerge with new strains that facilitate them to escape from present control measures. Emerging and re-emerging diseases arise due to genetic changes because of immunological pressure and recombinations with other viral or cellular genes. Currently, microbes and concerned vectors are changing themselves because of continuous change in agriculture versus animal husbandry practices. A faster mode of trades of animals and their products have facilitated the spread of microbes and the vectors involved; to newer zones of territories. The

possibilities of emergence of vector borne diseases can also be co-related with air travelling (Kumar et al., 2015a). Because of high urbanization, forest area is constantly shrinking which may result to lead more interaction between human, captive and wild lives resulting in emerging novel microbes. Sometimes, already existing organisms may transform into an actually novel, and until now unidentified organisms. Emerging diseases are more threatening to ruminants because of less information available about their origin, magnitude of economic losses as well as epidemiology. Recently, numerous resistant bacteria to many drugs are arising with unique pathogenic potential for human through food chain like *Campylobacter*, *Salmonella enterica*, *Enterococcus* spp. etc (Mishra et al., 2011; Kumar et al., 2015a).

6 Exotic Diseases

There has been a constant risk of emergence of novel pathogens/ diseases into a disease free country results in a grave effect on animal health due to high morbidity and mortality. Exotic (non-native) diseases/organisms, once entered into a country, can become more intense into an epidemic as being overlooked by the veterinarians due to its non-recognition or being prejudice of its non-occurrence. The disease may also intensify due to non-availability of suitable drugs or vaccine for control, the absence of disease resistance in the host and inadequate facilities in diagnose and limiting the spread of the disease.

Figure 1 Disease map and ruminant species affected. Different diseases and the species affected are shown in the figure. Map also represents the place and year of few diseases reported for the first time in India.

Therefore, it is needed to put extra precaution while importing the animals from disease suspected countries, which may harbour the pathogens. The WTO has granted permission to take legal actions in countries to implement their sovereign rights to save their livestock from fatal diseases (Bayry, 2013; Kumar et al., 2015a).

7 Diagnosis of animal diseases

A tentative diagnosis of the diseases can be done on the basis of clinical signs, species affected, epidemiological pattern, post-mortem lesions and laboratory confirmation by isolation of etiological agent, various serological and molecular methods. Serological tests such as counterimmunoelectrophoresis (CIE), agar gel immunodiffusion test (AGID) or agar gel precipitation test (AGPT), ELISA, complement fixation test (CFT), serum or virus neutralization test (VNT), hemagglutination (HA) and hemagglutination inhibition (HI) test are often used for diagnosis. Virus isolation, immunohistochemical detection, immunoperoxidase test (IPT) and indirect immunofluorescence test (IFAT), RT-PCR, real-time RT-PCR and nucleic acid hybridization are also commonly used for diagnosis of diseases (Rajeev et al., 2011). The novel proteomic techniques interventions like 2-D gel electrophoresis, HPLC and MALDI-TOF have also given better insight to the disease diagnosis by characterizing the microbes' aetiology (Balamurugan et al., 2014; Chakraborty et al., 2014; Dhama et al., 2014a).

7.1 Conventional tests/assays

The major disadvantage of the conventional assays is more labour and time consuming, less sensitive hence not suitable for proper diagnosis, however, used for secondary confirmatory diagnosis and retrospective epidemiological studies. To overcome the disadvantages of conventional assays, novel molecular biological techniques like real-time RT-PCR, loop-mediated isothermal amplification (LAMP) assays, and real-time LAMP have been developed and used frequently for the rapid and sensitive diagnosis of infectious RNA and DNA from clinical materials at nano and picogram level (Rajeev et al., 2011; Sharma et al., 2015). Out of these, for the diagnosis of the diseases, isolation of the microbes stands the gold standard. Virus/ bacterial isolation always cannot be performed as routine diagnostic tests since they are cumbersome, time-consuming, and need cell culture or other selective growth media facilities. Beside that the chances of missing the organism are more due to unfair handling while processing the samples. The traditional culture techniques are also not as sensitive as molecular tools like RT-PCR (Balamurugan et al., 2014; Chakraborty et al., 2014; Dhama et al., 2012).

Several researchers are undergoing towards the development of molecular diagnostics tools for the early, rapid and specific detection of diseases. For serological diagnosis of diseases and mass screening of samples for seromonitoring or

serosurveillance or clinical prevalence, ELISA is a rapid, simple and sensitive assay. MAb-based competitive ELISA (c-ELISA), immunocapture ELISA, sandwich ELISA (s-ELISA), simple and aqueous phase ELISA (SNAPELISA) and blocking ELISA (B-ELISA) are often used for disease diagnosis. ELISA has a higher diagnostic sensitivity and specificity for detection of antigen/antibody in samples (Afshar et al., 1989; Afshar, 1994; Balamurugan et al., 2014; Chakraborty et al., 2014).

7.2 Molecular diagnostic techniques

Due to the advent of improved biotechnological tools results in better understanding of the genome of pathogens and nucleic acid-based specific and sensitive assays were developed.

7.2.1 Nucleic acid hybridization

Nucleic acid hybridization has been widely used for the identification and differential diagnosis of diseases with the limitations of cumbersome and time-consuming, and feasible for regular diagnosis with number of samples. Despite high sensitivity, radio-labelled probes were not broadly used due to a short half life of ^{32}P , the risk of biohazard needs isotopes handling facility and fresh samples. To overcome disadvantages of radio-labelled probes, non-radioactive probes were developed using digoxigenin (DIG) labelled oligonucleotides or biotinylated DNA. This test provides very specific and rapid results moreover its sensitivity is also not less than that of radioactive labelled probes (Rajeev et al., 2011; Sharma et al., 2015). Some more advance assays like Fluorescent in situ hybridisation (FISH) can also be used to localise the targeted nucleic acid sequences within the cellular material (Balamurugan et al., 2014; Chakraborty et al., 2014).

7.2.2 Polymerase chain reaction (Nucleic acid amplification)

RT-PCR has been commonly used for detection and differential diagnosis of diseases. The two-step and one-step RT-PCR has been commonly used for the rapid diagnosis of RNA and DNA in the clinical samples in a single step, which has the capability to replace the existing PCR. A highly sensitive RT-PCR-ELISA for the diagnosis and differentiation of diseases has been developed using RT-PCR product labelled with DIG. The test can identify viral RNA with a titre minimum of 0.01 TCID₅₀/100 µl in the infected tissue culture fluid. PCR-ELISA is 10,000 times more sensitive than RT-PCR for identification of early and late stages of infection (Rajeev et al., 2011; Sharma et al., 2015). For rapid specific detection and quantification of antigen, real-time PCR techniques targeting genes of pathogens was developed using SYBR Green or TaqMan hydrolysis probe, which is highly sensitive. Multiplexing of Real Time PCR technique can curtail the time further as able to quantify more than single aetiology in one run (Afshar et al., 1989; Afshar, 1994; Balamurugan et al., 2014; Chakraborty et al., 2014; Dhama et al., 2012).

7.2.3 Pen-side tests

In the recent years, rapid, simple, specific and highly sensitive novel field diagnostic device known as latex beads based agglutination tests (Rana et al., 1999) and LAMP (Loop-Mediated Isothermal Amplification) were developed. This test provides a rapid and sensitive diagnosis in a rural environment, where no laboratory equipment was available. LAMP can be performed where thermocyclers cannot be easily maintained/procured (Rekha et al., 2014). The advantage of these tests is no need of agarose gel electrophoresis. Lateral flow test (Arun et al., 2014), simple dot-ELISA, dipsticks, immunofiltration, and antigen-competition ELISA were developed for the diagnosis of antigen/antibody in samples. These tests can be used for screening of large number of clinical samples and suitable for animal disease diagnosis in the field and can be used as a pen-side test for identification of disease. A suitable LAMP test was developed for the diagnosis of *Mycoplasma agalactiae* the causative agent of contagious agalactia in goats with the detection level of 20 fg DNA. The test could be performed with 70 min. at 58°C constant temperature (Rekha et al., 2015). These assays had high diagnostic sensitivity and specificity and bear the advantages of rapid, user-friendly, more economic and do not need technical skill or expertise (Balamurugan et al., 2014; Chakraborty et al., 2014; Dhama et al., 2014b; Sharma et al., 2015).

7.2.4 Recombinant antigen-based assays

Nowadays, production of recombinant proteins becomes simple and more efficient, due to the progression of recombinant DNA and gene expression technology. Due to the advantage of genetic modification, the quality and quantity of recombinant proteins became improved and the maintenance of post-translational modifications usually determines the choice of the host systems. Various efforts have been made to develop the different expression systems like bacterial, mammalian, yeast and insect cells for expression of different proteins of pathogens and to evaluate the possible use of recombinant proteins in different diagnostic tests. The limitations lay here with that of biosafety issues which need to be taken utmost care (Balamurugan et al., 2014; Chakraborty et al., 2014; Sharma et al., 2015).

7.2.5 Nanotechnologies

The tests involved here are able to detect molecular interactions. The benefits of such tests are their smaller dimensions by using nanoarrays and nanochips as platforms. Another superiority of such arrays is their potential to analyse a sample for an array of all the probable infectious agents which are having common overlapping clinical signs in single DNA chip. The technique is of use in detecting Influenza strains and vesicular viral diseases. Beside that the nanoparticles like gold nanoparticles, nanobarcodes, quantum dots (cadmium selenide) labelled antibodies/ antigens are also used for identification of specific pathogens or molecules

(Rajeev et al., 2011; Balamurugan et al., 2014; Chakraborty et al., 2014; Sharma et al., 2015).

7.2.6 Biosensors

Biosensors based assays are the tools used either to detect antigen or an antibody. In such assays, there is a use of receptor (antibody) as well as a transducer which converts a biological interaction reaction into a quantifiable signal. The common transducer technologies are electrochemistry, fluorimetry, reflectometry and/ or resonance. The Biosensors are attached to very high sensitive instruments able to capture readable signals. The limitations of such applications are as it needs high skilled persons for interpretations of the result, the high cost of equipment and high sample processing charges (Balamurugan et al., 2014; Chakraborty et al., 2014; Rajeev et al., 2011; Sharma et al., 2015). Diagnostic techniques used for the diagnosis of different diseases along with their merits and demerits are presented in Fig. 2.

8 Strategies for prevention, control and eradication of diseases

Generally, for prevention, control and eradication of infectious diseases, strict biosecurity measures, quarantine, and isolation of infected and disease suspected animals should be appropriately implemented. Added these, effective disease surveillance, monitoring and networking programmes with suitable vaccination and treatment strategies are of utmost importance for the successful control of various diseases (Dhama et al., 2013b; Dhama et al., 2014b; Verma et al., 2014b). Supported with conventional diagnostic tools, recent advancements in diagnostics viz., multiplex PCR, LAMP, biochips, microarrays, nanotechnology, gene sequencing and phylogenetic analysis need to be strengthened for early and confirmatory diagnosis of ruminant diseases (Kawadkar et al., 2011; Dhama et al., 2012; Dhama et al., 2014a; Dhama et al., 2014b; Hurk & Evoy, 2015; Karthik et al., 2016).

Together with conventional live and killed vaccines in practice, recent advances in the field of vaccines and vaccinology need to be exploited to their full capacity to counter important diseases of ruminants and help alleviate economic losses of animal producers. These include DNA vaccines, subunit vaccines, recombinant vaccines, plant/edible vaccines, virus-like particles, nano vaccine etc. (Dhama et al., 2008; Dhama et al., 2013c; Delany et al., 2014; Finco & Rappuoli, 2014; Kim et al., 2014; Singh et al., 2014c; Pany et al., 2015; Singh et al., 2015b). Along with this, for designing, developing and producing effective vaccines the usage of modern adjuvants (TLRs), immunomodulators, and delivery systems is the need of the hour for providing better protection to animals after vaccination (Reed et al., 2013; Dhama et al., 2015b; Singh et al., 2015b).

Flaring up of several emerging and re-emerging diseases due to several predisposing factors including immune pressures, evolution and mutations in microbes, global warming and rising drug resistance in microbes also demands research attention for exploiting alternative and promising therapeutic options of probiotics, cytokines, si-RNA, egg yolk antibodies (IgY), phages, toll-like receptors, nanomedicines, herbs and nutritional immunomodulators (Blecher et al., 2011; Dhama et al., 2013d; Dhama et al., 2013e; Dhama et al., 2014a; Dhama et al., 2015b; Mahima et al., 2012; Malik et al., 2013c; Tiwari et al., 2013; Tiwari et al., 2014).

In spite of huge coordinated efforts for the eradication and control of animal diseases like CBPP, RP, and FMD, until now in India rinderpest is the only disease successfully eradicated (Sekar et al., 2011; Bayry, 2013; Balamurugan et al., 2014). India was declared provisionally free from Contagious Bovine Pleuropneumonia (CBPP) from October 2003, however from May 2007, OIE declared India free from CBPP infection

(Singh & Rana, 2014). Similar attempts are required to control and eradicate the enzootic diseases present in India, which causes more economic losses every year. The disease control programmes in India includes National Control Programme on Brucellosis (NCPB), Foot-and-Mouth Disease Control Programme (FMDCP), avian influenza, preparedness, control and containment, and National Control Programme of Peste des Petits Ruminants (NCPPPR) could not be progressed up to satisfactory level further. In the 12th five year plan, the focus is also given for monitoring and control of certain economically important animal diseases (Sekar et al., 2011). There should be strict implementation on controlled movements/ transport of animals from one state to another as well as strict quarantine measures should be adopted. As being a tropical status of the country, more emphasis should be given on the research and development work for Thermo-durable vaccines so that the dependency over cold chain may be avoided and effective vaccination programme can be implemented (Singh et al., 2009b; Verma et al., 2014b; Sharma et al., 2015).

Figure 2 Diagnostic techniques used for diagnosis of different diseases, their merits and demerits.

8.1 Mass vaccination is a key for disease control

Mass vaccination has been the practical approach for control and eradication of several infectious diseases worldwide. In humans, for the control and eradication of polio, mass vaccination approach was followed by World Health Organization (WHO). Few successful examples are smallpox and polio in humans and rinderpest and CBPP in cattle. Effective control measures along with proper vaccination will get rid of the epidemics of livestock diseases (Sekar et al., 2011). Vaccines will safeguard the livestock by decreasing the spread of infectious agents. Recent molecular advancements like reverse vaccinology resulted in the development of subunit DNA, recombinant and non-pathogenic virus-vectored vaccines leads to production of economically feasible low cost vaccines that are used at field level. In rural areas, basic infrastructure facilities like cold storage needs to be established in veterinary dispensaries to offer improved livestock health services (Bhanuprakash et al., 2010; Bhanuprakash et al., 2011; Dhama et al., 2014a). More work needs to be done in the area of cheaper vaccine development, so as to attract more and more livestock owners to get their animals vaccinated.

8.2 OIE pathway

Due to social, ethical and political reasons, restriction of animal movement and test and slaughter policy are difficult to follow in India. Mass vaccination strategy is the feasible, best viable and economical method for control and eradication of diseases (Verma et al., 2014b). India has successfully eradicated the rinderpest by adopting the OIE pathway and in future for successful eradication of any enzootic diseases and to announce the country free from diseases, it is necessary to follow the OIE pathway. OIE pathway includes initial mass immunization, followed by serological surveillance for two years and then no vaccination. These approaches definitely push the country towards free from enzootic diseases results in the declaration of provisional absence of disease. To attain total disease eradication status in the nation a request/report needs to be submitted to the OIE to officially announce as free from disease, after 3 years of the initial declaration. Two consequent yearly serological screening are necessary during this 2 year period. Therefore, a total of 8 to 10 years is needed for officially to declare any disease free from a particular country (Singh et al., 2009b; Verma et al., 2014b; Sharma et al., 2015). It is essential to keep the disease database and disease registry to confirm efficient reporting and monitoring of disease outbreaks. The trained technical, scientific, supporting manpower is required to run a successful disease control program. Surveillance is an effective tool to undertake the disease control program along with mass vaccination. Effective disease forecasting models and programmes need to be developed which have applied applications. These sound models may generate a high confidence level among stakeholders. Further, this may incline them more towards adopting animal husbandry practices to earn their livelihood (Sekar et al., 2011). Veterinarians and para-veterinarians are required to be trained and equipped for rapid diagnosis of

disease and reporting actions at the district level. The clinicians and diagnostic laboratory personals have to collect the samples from various places frequently like animal fairs, veterinary hospitals, slaughterhouses and livestock farmers who are the direct stakeholders (Singh et al., 2009b; Verma et al., 2014b; Sharma et al., 2015).

8.3 Cost analysis of control program

India is still developing the country, analysis of cost for control program is essential. For the implementation of control and eradication program for any diseases needs a considerable amount of financial support from the Government of India. Any disease control programme needs fund for vaccines production and/or purchase, manpower (scientific, technical and supporting), diagnostics, equipment, contingent expenses and infrastructure. In some circumstances, manpower can be arranged by state veterinary departments, research institutes, and colleges. Further to reduce the cost infrastructure facilities developed during the execution of the National Project on Rinderpest Eradication (NPRE) could be used for any disease control and eradication programs after required up gradation (Singh et al., 2009b; Verma et al., 2014b; Sharma et al., 2015).

8.4 Public-private partnership (PPP)

A lot of successful stories are available regarding public-private partnership in India like ongoing polio control and eradication program. Various non-governmental organizations (NGOs) are significantly contributing to animal husbandry development programmes all over the India. Veterinary vaccines and other biological products are produced by government organizations belonging to both state and central in India. In India, there are 29 biological (vaccines) production centres, among which 22 are under the control and aid of government and 7 are under the control and aid of private sector. Further, many cooperatives are actively contributing for vaccinations, deworming, housing and sheep/goat breeding in many states. The involvement of cooperatives and NGOs are necessary to run the control and eradication programs of diseases. The livestock population is more in India, a large volume of vaccines is needed to implement the programme and hence it is essential to have an association with private manufacturers. Moreover, various NGOs and top private vaccine manufacturers voluntarily undertake the low-cost vaccine production technologies, for launching the control and eradication program (Singh et al., 2009b; Verma et al., 2014b; Sharma et al., 2015).

8.5 Social and Political Concerns

Another most important success-determining factor is the political support for disease eradication programmes. To involve the political support, the selected disease for eradication should be need based, economical, international relevance, zoonotic priority and technically feasible. Therefore, clear goal and commitment at various levels are necessary especially in the field staff should be created awareness

regarding goals and modalities and should be motivated with incentives. The important social requirement for disease eradication programmes from livestock farmers is perseverance. Presently, both social and political importance of many diseases have been understood and could more be taken advantage to support the disease eradication programme at an international level (Singh et al., 2009b; Sharma et al., 2015; Verma et al., 2014b).

8.6 Constraints in eradication of disease

Initially, the incidence of the disease in animals is reported by the village livestock farmers or sarpanch of the village or local village assistant to field veterinarians. At that time, the disease is diagnosed on the basis of clinical signs described by the livestock farmers and majority of infected animal dies by the time veterinarian reaches to the village due to insufficient transport facilities. Due to this limitation, a collection of samples from infected animals and subsequent confirmation of the disease would not be possible. Further, many outbreaks of the disease are not reported frequently, hidden and affected animals were sold at low cost. The areas where a veterinarian can arrive the animal before removal, they are unable to collect the samples because of lack of facilities for collection, preservation and transportation to the adjacent laboratory for diagnosis (Chakraborty et al., 2014; Dhama et al., 2014a). A major problem in the control and eradication of diseases using test and slaughter policy is inadequate compensation to the owner for the culling of infected animals. This encourages the owners to hide the clinical sign of the disease in affected areas results in the existence of the disease and animals will act as carriers (Verma et al., 2014c).

8.7 Disinfection of the infected animal premises and their products

Materials and by-products from infected animals like meat and meat products, offal, wool, skin, and hide should be thoroughly disinfected by chemical inactivation, heat treatment, and ionizing irradiation. Milk and dairy products from infected/suspected animals need to be disposed off. Bedding materials from infected animals, feed stuff, excretory and secretory products including dung and urine, and clothing of person working in infected animal houses should be destroyed properly (Chakraborty et al., 2014; Chand et al., 2015).

8.8 India's Potential to control and eradicate the diseases

India is a developing country, with 29 states and 7 union territories. The veterinary infrastructure facilities for control and eradication of diseases were available at both central and state levels. A total of 8732 veterinary hospitals (polyclinics), 18,830 veterinary dispensaries and 25,195 veterinary aid centers/stockhome centers/mobile dispensaries were available in the country (Bhanuprakash et al., 2011; <http://dahd.nic.in/>). In addition, India has 53 veterinary colleges, and 13 veterinary and animal science universities distributed throughout the

country. Further, more than 31 non-governmental organizations (NGOs), 642 Krishi Vigyan Kendras (KVKs) and 23 state biological units were available in the country. Veterinary and animal science has the supreme apex body called as Indian Council of Agricultural Research (ICAR) under which 9 national institutes in the country like, Indian Veterinary Research Institute (IVRI) and National Dairy Research Institute (NDRI), etc., 2 Project Directorates, 6 National Research Centres and one National Bureau of Animal Genetic Resources are there. ICAR is the central organization to plan, implement and execute the control programs with the help of department of animal husbandry under the ministry of agriculture and animal husbandry. The main referral laboratory for disease diagnosis is Centre for Animal Disease Research and Diagnostic (CADRAD), which connects the regional disease diagnostic laboratories (RDDLs) located throughout the country at four zones namely south, north, east and west (Bhanuprakash et al., 2011). With the support of these facilities, India has the potential to control and eradication of diseases in future like rinderpest. India has been declared provisionally free from CBBP from October 2003 and OIE have declared freedom status of India from CBPP infection from May 2007 onwards. Likewise, other animal diseases like foot-and-mouth disease, PPR, Bluetongue, HS, brucellosis, etc., are possible to control and eradication in the future (Bhanuprakash et al., 2011; Verma et al., 2014b).

Conclusion and Future Perspectives

The animal diseases present in India require a serious attention and needs improved research facilities especially in the field of epidemiology and huge funding. Valid, state-wise, comprehensive research data especially in the field of epidemiology are necessary for planning and control of diseases that are endemic in India, otherwise implementation of control measures will be difficult and eradication will be impossible. Animal diseases are not only danger to the Indian economy but also equally important in respect to the human health. During the recent years, majority of the infectious emerging diseases affecting the human are originated from animals. Thus, it is logical to say safeguarding the animal health is most important for maintenance of human health. For successful control of diseases, epidemiological forecasting, quick and correct diagnosis, safer and quality vaccines, sanitation measures along with adequate infrastructure facilities for cold storage and transport facilities to reach the vaccines for the remote areas, where end users are living; are necessary. Advanced diagnostic assays have reduced the puzzle in the diagnosis and differentiation of diseases from others. Door delivery of veterinary services and better extension services for greater awareness to farmers will significantly enhance the possibility of eradication of diseases thus helping in control programmes. The major constraints in the control of disease in the developing country like India are poor vaccination coverage, lack of financial support and insufficient infrastructure, which interferes the building of herd immunity. An interdisciplinary approach like veterinarians, scientist (animal health), medicos, para-veterinary officers, and

NGOs need to take a leadership role while implementing the control programmes for controlling and eradication of important diseases of livestock. This will increase the livestock production and their sustainability, which ultimately results in alleviation of poverty in the rural areas of the country.

Conflict of interest

Authors would hereby like to declare that there is no conflict of interests that could possibly arise.

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