Review Article

Control of Paratuberculosis: Opinions and Practices

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Abstract | Johne's disease (JD) or Paratuberculosis is one of the most wide-spread, highly prevalent and economically devastating infectious diseases of domestic livestock worldwide. It is caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP). Disease is endemic in the domestic livestock, and is a spectral disease characterized by long sub-clinical phase without signs of infection. Therefore control of disease is difficult and offers challenges at both scientific and management levels. Since disease is incurable, control of paratuberculosis has emerged as a new science and is continuously evolving in last two decades. Present paper reviews the National disease control programs that are in practice in different countries around the world.

Keywords | *Mycobacterium avium* subspecies *paratuberculosis*, Johne's disease, Control practices

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INTRODUCTION

Johne's disease (JD) or Paratuberculosis has recently emerged as one of the most wide-spread, highly prevalent and economically devastating infectious diseases of domestic livestock around the world (Singh et al., 2014a). Disease is caused by an extremely fastidious microbe known as *Mycobacterium avium* subspecies *paratuberculosis* (MAP). Disease is globally distributed and is endemic in the domestic livestock (Figure 1 and 2). MAP is highly resistant to environmental stresses like temperature and drying, and is able to persist for years in farm soil (Singh et al., 2013). Infected animals (sub-clinical and clinical) excrete huge quantities of bacilli in their feces, milk, semen, uterine fluids etc. Animals get infection of MAP either through semen or in fetal life during pregnancy or at birth through suckling of mother (colostrum and milk) or later in life through contaminated feed and environment (Ayele et al., 2001). Though *in utero* (vertical) transmission of disease has been established, however semen and embryo transfer are also known to play important role in disease transmission (Khol et al., 2010). In infected herds/flocks, all the animals get exposed to MAP soon after birth by fecal-oral route (Ayele et al., 2001). Free ranging and wild animals have also been considered as reservoir of MAP for farm animals (Singh et al., 2012). Paratuberculosis is a spectral disease characterized by silent, sub-clinical, clinical, advance clinical and terminal stages. First

two phases of the disease are asymptomatic in nature. Incubation period may last several years before the onset of clinical disease and some animal may remain asymptomatic for whole of the life. In the absence of frank clinical lesions and a spot test, diagnosis of disease is extremely difficult especially in early stages of the disease. Therefore asymptomatic animals continue to shed MAP in their feces and are constant source of infection to susceptible and naïve animals in any population (herd / flock).

MAP exists in several biotypes / genotypes (Sohal et al., 2010a), which can cross-infect different host species (Sohal et al., 2010a). Different animal species are susceptible to different bio-types of MAP, which makes control of this disease extremely difficult. Indian studies in last one and a half decade have reported extensive presence of 'Indian Bison Type' bio-type, which is a new bio-type (Sohal et al., 2010b) and has not been reported from any other country in the world outside India (Singh et al., 2014b). This new bio-type has been reported exclusively from sheep, goats, buffaloes and wild animals in India and has also been shared by other domestic livestock species like cattle, other animals like rabbits and primates including human beings.

Control of chronic diseases like Paratuberculosis is a daunting task in several ways. Firstly, due to the absence of specific clinical symptoms in affected animals. Secondly, due to lack of sensitive and specific diagnostic tests and reagents to diagnose JD in sub-clinical stage pose difficulty in timely control of the disease. Thirdly, due to lack of effective vaccines for the prevention of disease adds to the grave situation of the disease in many countries around the world including India. Though number of vaccines have been claimed to reverse the clinical disease and reduce fecal shedding of MAP, but many of the multi-country and global vaccines under different management conditions does not hold same promise as in the native situations of the disease in the country of the origin.

At present, the chemo-therapeutic options are extremely few; moreover, presence of drugs and drug residues in milk and meat of animal are no longer acceptable to consumers since these drugs reach human beings via food chain. Considering all these factors, effective control of the disease is not only difficult but also invites trade restrictions. Therefore, all the developed countries in the world have 'National programs' in place for control of John's disease with aim to survey, diagnose and control this incurable disease. This paper reviews the opinions and practices followed for the control of JD in different countries/parts around the world.

CONTROL PRACTICES

Production losses caused by paratuberculosis infection in dairy and meat animals vary in different countries due to variations in the animal husbandary practices and economic conditions of these countries and susceptible species/breeds. Developed countries around the world have adopted different programs for the control of this disease as per their technical skills, financial capacities and administrative will. Johne's disease is still a low priority disease in many developing and poor countries including India. Johne's disease is yet to conceptualize as the impending threat and challenges the disease pose to the both animal and human population around the world. Livestock species (goats, sheep and buffaloes) which can be slaughtered, go for early slaughter and these animals remain for very short time (2-3 parturitions) in the production system, leading to wastages and burden on nutritional resources due to reduced feed conversion efficiency and increased non-productive conditions (late maturity, increased inter-calving period, early culling etc.), therefore leads to increased methane emission. Globally, there is lack of an 'international program' either for the control or eradicatation of this incurable disease of domestic livestock. However, management of disease by culling of infected animals has not given any dividends in coutries where it has been in practice for long time, since disease is transmitted vertically from infected parents to new generation. Most of the developed countries have adopted rigorous practices (hygiene, management, vaccination) for the control and elimination of paratuberculosis infection from their herds and flocks and have succeeded in boosting per animal productivity and decreasing the production losses year by year.

Control Practices in United States (http://www.johnesdisease.org/)

In United States, 'National Animal Health Monitoring System' (NAHMS) is a system for studying the prevalence and economic losses caused by different animal diseases including JD. As per 1997 survey report on dairy herd prevalence of disease was 30–50% and

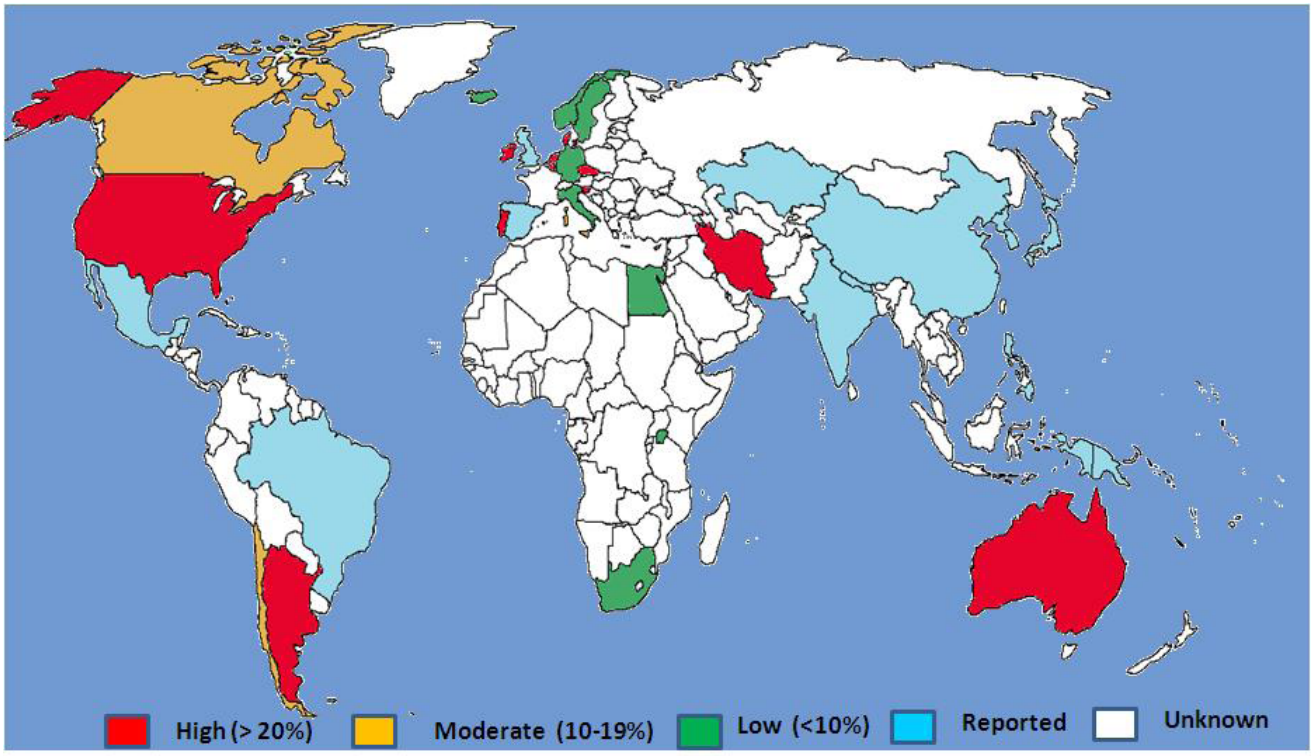

Figure 1: Global distribution of Johne's disease in domestic livestock species

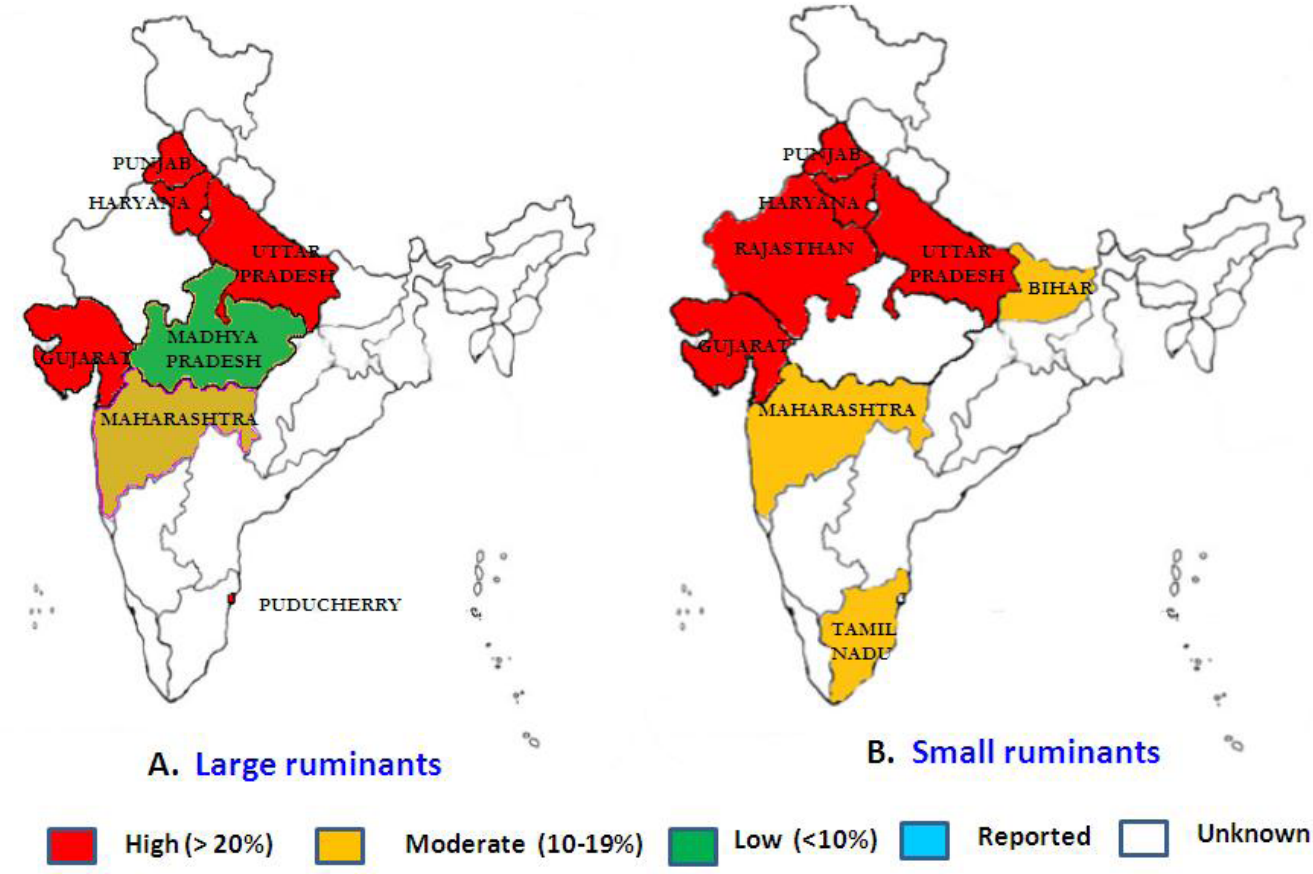

Figure 2: Distribution of Johne's disease in India

reports from slaughterhouse surveys showed 7–18% of cattle in US to be infected by MAP. Therefore, for the control of this disease, the 'Voluntary Bovine Johne's Disease Control Program' is being implemented. This

Program is the coordinated effort of National Johne's Disease Working Group and the Johne's disease Committee of the United States Animal Health Association, State veterinarians and industry representatives, and has been recognized by the USDA's Animal and Plant Health Inspection Service (APHIS). Program is run by the state and is supported by industry and Federal Government. Producers are encouraged to participate in the voluntary programs. Components of control programs include: 1) Education of farmers and veterinarians, 2) introduction of best management practices, and 3) Herd diagnosis. Producers decide their level of participation; Education component or Education and Management components or Education, Management and Testing without Herd Classification or Education, Best Management and diagnosis to obtain a Herd Classification Level. By participating in this program, producers have opportunity to achieve a Classification Level.

Control Practices in Australia (http://www.animalhealthaustralia.com.au/njdcp)

'National Johne's Disease Control Program' (NJDCP) has been formulated in Australia to help livestock industries in controlling JD and is managed by Animal Health Australia. It is a collaborative program involving livestock industries, government bodies and the veterinary component. NJDCP focuses on limiting the spread of this disease between areas by training, extension and diagnostic methods. Key components of this program are: 1) Development of National Standards, 2) Johne's Disease Market Assurance Program, and 3) Diagnostic Procedures. National standards controls the individual program in respective states, Market Assurance Programs encourages producers to participate in the control programs. Australia is also using inactivated vaccine (GUDAIR) for control of ovine Johne's disease and save their wool industry.

Control Practices in New Zealand

Deer industry in New Zealand is concerned about the on-farm impact of paratuberculosis, and the consequences for the foreign market. Research is thus directed at investigating tools for paratuberculosis control to reduce the threat to the industry. The three methods of the control measures that are being implemented in New Zealand are Test and cull, management interventions and development and use of vaccination (Stringer, 2010). Program for developing indigenous vaccine for deer population are in full swing.

Control Practices in Denmark

Paratuberculosis in Denmark is a widespread disease. Voluntary control program was established in 2006 to control the spread of this disease. Danish Cattle Federation decided to launch a control program, 'operation paratuberculosis' in 2006 (Nielsen, 2007). Recommendations for reduction of transmission of MAP were based on protecting calves against manure from adult cattle e.g. removal of the new born calf immediately after calving, and calving takes place in special calving pens, which are cleaned after each calving. These management measures were recommended to prevent fecal material from cows getting in direct contact with susceptible calves, irrespective of the infectious status of cows.

Control Practices in Sweden

In 1952, Johne's disease was included in the Swedish Epizootic Act (Sternberg et al., 2007) and any suspicion of this disease is notifiable for animal owners. In the case of detection of any infected herd, stamping out policy is applied followed by extensive tracing of all contact herds / flocks. Entire premises of the herd are thoroughly cleaned and disinfected, and a holding period is applied on the buildings, pastures and farmland.

Control Practices in Netherlands

Epidemiological and economical modelling based on cost benefit and risk assessment is the basis of control program in Netherlands (Franken, 2005). Dutch Paratuberculosis Program was started in 2000 with an aim to control paratuberculosis and its effect on profitability. Livestock industry and the Government are partners in this program. Ministry of Agriculture, Nature Management and Fisheries, the Ministry of Human Health, the Commodity Board, the National Dairy Organization, the Animal Health Organization and the Dutch farmer's organization are partners in this program. The Animal Health Service is responsible for executing the program.

Control Practices in Czech Republic

Culling of animals based on results of ELISA and fecal culture twice a year for animals about 1.5 years is the basis paratuberculosis control in Czech Republic. The costs of these tests are paid by the government (Pavlas, 2005). The loss of animal is either covered by the herd owner or by his insurance company.

Control Practices in Canada (www.animalhealth.ca)

Canadian dairy herds, the dairy industry, government, and veterinary schools have collaboratively created the Canadian Johne's Disease Initiative (CJDI) to decrease the prevalence and economic consequences. Education and management is the basis of this program. Depending on the individual preferences and herd / flock structures, herd owners and veterinarians decide on a plan for management practices. Therefore, different provinces have launched different programs to control paratuberculosis. All of the programs have key elements in common. These include education of farmers and veterinarians, farm risk assessment, testing at either the herd or the cattle level.

Control Practices In United Kingdom (http://www.checs.co.uk/)

In UK, Cattle Health Certification Standards (CHECS) has licensed about 10 control programs. These programs require annual testing of cattle >2 years with serum ELISA or individual fecal culture or PCR. Herds with negative status gains 'Level 2 one year clear' classification then progress annually for 3 years to level 1. After maintaining level 1 status for 2 years, the test interval becomes biennial. CHECS licensed programs requires removal of test positive animals, removal of recent offspring of test-positive animals, minimizing fecal contamination of feed and water resources, preventing co-grazing with other animals, providing an isolation facility, preventing grazing of potentially contaminated pasture, supply of mains water only, disinfection of shared equipment and facility. Vaccination is advised for herds with high clinical prevalence.

Control Practices in India

India had policy of testing of animals mainly cattle against Johne's disease and bovine tuberculosis since 1950s and provisions of segregation of positive and negative animals was made using Johnin and tuberculin. Since cattle cannot be slaughtered, the policy of maintaining JD infected (positive) animals in isolated herds was made but due to recurrent increase in the cost of maintenance and constrains in the funding, the program slowly. At present, the Government of India does not have any program for the control of Johne's disease. As a result, per animal productivity of Indian domestic livestock is very low even in Asian countries (1/6th). However, at some of the government farms of goats and sheep, the policy of 'test and removal' has been followed for last 30 years but without much impact on the prevalence of infection or disease in the herds and flocks. These small and isolated efforts that too at few government farms are too insufficient to make any impact in controlling the disease in major population available with small and marginal farmers. India is home to the highest population of goats, cattle and buffaloes and 3rd highest population of sheep in the world however, majority of the animals of the four domestic livestock species are very low producers mainly due to JD. Since cows cannot be slaughtered legally due to ban on cow slaughter, sacred cows once off production are left out by the farmers and roam around on the roads. If other species of animals (goats, sheep, and buffaloes) are off production due to JD or become weak and emaciated, go for early slaughter for meat production and this way have some salvage value. Therefore, population of these 3 livestock species is continuously increasing in last more than 6 decades, in comparison to cattle. In the absence of control measures, incidence of JD is also increasing continuously in last 30 years (Singh et al., 2014b). Un-hygienic conditions and poor sanitation at livestock farms, non-composting of animal excreta / waste, absence of policy for the control and management of JD in animals, increasing use of pasteurized milk for making variety of food items such as ice-creams, milk powders, condensed milk, flavoured milk and curd, butter milk etc., is creating a niche for MAP and a vicious cycle of movement of MAP from animals to soil and water (environment) and back to animals and human beings. Hence JD control programs are the immediate requirements of the country in order to boost per animal productivity.

However, designing of control programs will depend on the prevalence (bio-load) estimates and economic losses in livestock production system (Singh et al., 2014b). Initiation of control measures at National level will not only help in boosting farm output but also optimum use of scarce and costly nutritional resources by optimizing productivity of native breeds, thereby making animal husbandry if not a profitable but at least a sustainable venture.

OPINIONS ON THE CONTROL OF JOHNE'S DISEASE

Johne's Disease being an infectious disease which is

transmitted both vertically and horizontally, therefore status of infection in herds and flocks of domestic livestock species with time continue to increase. If interventions to control are not applied bioload of MAP may reach alarming propositions. Hence, various opinions have been put forward as the control program for this disease at global level:

- Disease should be managed as herd/flock problem rather than as health problem of individual animals.
- Introduction of MAP into a herd / flock occurs through entry of new infected animals, mostly sub-clinical. Therefore, animals must be quarantined before inclusion into the herd and farmers should buy animals from 'un-infected ('test-negative) herds' as replacement stock.
- In an infected herd, exposure of susceptible/ healthy animals must be reduced by separating infected animals and timely removal /culling.
- In infected herds and flocks, young and new borne animals must be segregated and should not be exposed to contaminated manure, colostrum and milk. Milk and colostrum should not be pooled. Milk should be heated to boiling point before feeding to the calves.
- Herds must be periodically tested for appearance of positive and clinically infected animals. Infected animals must be separated, segregated and culled.
- Breeding of infected animals should be restricted. If not so; the new born animals from infected mothers should be removed.
- Young animals should be reared separately from adults. Grazing of young animals should be delayed, if possible for at-least one year.
- Stress to animals must be minimized to maintain their health and immunity.
- Manure build up in and around farm premises should be prevented, and feed and water resources should also be provided from the elevated platforms to reduce environmental contamination.
- Young animals should be prevented from contamination through contact with adult stock or environment (water, soil, manure, pasture land etc).
- Farm animals, paddock, grazing lands etc. should not be accessible to wild animals specially ruminants.
- Surfaces should be thoroughly cleaned with soap, followed by tuboricidal disinfectants.

In the era of increasing global trade options, ecosystem and biodiversity changes, increasing population and emerging antimicrobial resistance, there is immense need for developing effective and novel /alternative therapeutics and better vaccines along with immunomodulatory modules by strengthening various Research and Development programmes to counter Johne's disease and its public health concerns (Kahn et al., 2007; Meeusen et al., 2007; Dhama et al., 2008, 2013a, 2013b, 2013c, 2014a; Mahima et al., 2012; Koff et al., 2013; Tiwari et al., 2013, 2014; Singh et al., 2014a; Verma et al., 2014). This also requires follow up of the real concepts of One world One health One medicine, international co-ordination and networking, adapting advances in disease diagnosis and control measures and implementation of good management practices including strict biosecurity practices (Schmitt and Henderson, 2005; Bergquist, 2011; Bollo, 2007; Deb and Chakraborty, 2012; Dhama et al., 2013d, 2014b; Singh et al., 2014a).

CONCLUDING REMARKS AND RECOMMENDATIONS

Johne's disease has received highest priority for management and control at National level in most of the developed countries and western countries around the world. JD control programs are in place in each of these countries, which are supported by Governments or livestock industries or the farmer's / producers associations. These countries have the advantages of good hygiene and sanitary conditions, low density of animal and human population, proper management system for livestock production through large farms, better health care, better nutritive feeding regimens, high per animal productivity, minimum social or religious interference in animal health and production management, which helped in the control of JD in their livestock farms.

However, condition of the animal husbandry is far from satisfactory level in major parts of the world which include most of the developing and poor countries. In the absence of initiative, lack of understanding of disease and losses, poor resources in terms of technical man-power, infrastructure of good laboratories, proper animal recordings, identification of individual animals, ban on cow slaughter (India), the bioload of MAP continues to increase in these countries resulting in low per animal productivity and increase chances of human infection. Therefore, global efforts

are needed in fighting this disease with active help of global organizations like OIE so that global efforts are initiated by including all countries to join hands for eradication' of the Johne's disease from the face of the earth.

Vaccine has been successfully used for control and eradication of diseases like Rinder pest, Foot and mouth disease in animals, and small pox and polio in human beings in the world. Therefore globally major initiative for the control and eradicate the Johne's disease in domestic livestock population should be through use of vaccine in order to save human population from infection.

CONFLICT OF INTEREST

No conflict of interest to declare.

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