Paratuberculosis; A Potential Zoonosis

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ABSTRACT

Paratuberculosis, commonly known as Johne's disease (Yo'-nees), is primarily a disease of ruminants such as cattle, sheep and goats. It is a chronic infectious disease. The name of the disease is derived from the scientist's name who discovered it in 1985 named Johne's along with his colleague Frothingham. The disease is associated with Mycobacterium avium subspecies paratuberculosis (abbreviated as MAP) is an obligate intracellular organism. This bacterium mainly damages the intestines. MAP is a member of Mycobacteriaceae family which also includes M. tuberculosis and M. leprae, causative agents of tuberculosis and leprosy, respectively. Paratuberculosis is also known as "Silent slayer" in USA. The prevalence of this disease is continuously increasing every year due to lack of proper disease control programmes. The reasons behind could be lack of awareness in public as well as the lack of concern shown by respective governmental disease control authorities. Paratuberculosis is chronic in nature due to which there is no accurate treatment for it. The transmission source for this disease is the infected animal. There is an ongoing uncertainty regarding its transmission to human as various researches have produced contradicting results. Its prevalence rate varies in different regions of the world however; it is found most commonly in the countries having intense livestock farming. Crohn's disease (CD) is the term used for the disease in human where the clinical symptoms are similar to those seen in John's disease in animals. MAP is considered the primary cause of CD along with other associating factors however it is yet not confirmed. Primarily, the consumption of dairy products, obtained from infected animals, is considered its mode of its transmission to human. Actual burden of CD is yet unknown as it goes unreported in most of the countries due to lack of awareness among the people & lack of sufficient funding for research purpose. Interdisciplinary research collaborations are necessary to cover the knowledge gaps regarding paratuberculosis, highlighting the significance of surveillance and preventive measures to reduce possible health hazards to people.

Key words: Johne's Disease, Emergent Zoonosis, Threat, Public Health, Crohn's disease.

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1. INTRODUCTION

Paratuberculosis, also known as Johne's disease (Yo'-nees), is a chronic infectious disease that primarily affects ruminant animals, such as cattle, sheep, and goats. History of Johne's disease goes back to the end of 19th century when couple of scientists named; Johne's and Frothingham (Whittington et al. 2019), described it for the first time in 1985. It is caused by Mycobacterium avium subspecies paratuberculosis (abbreviated as MAP) that mainly damages the intestines. MAP is a member of Mycobacteriaceae family which also includes M. tuberculosis and M. leprae, causative agents of tuberculosis and leprosy respectively. The organism is capable of surviving in the environment for a long time posing a continuous threat to all the susceptible species (Hovde and Moum 2012). Since it is an obligate intracellular organism, it always requires a cell named as; Macrophage, within the susceptible host, for its multiplication.

'Silent slayer' is the term used for this disease in USA (Whittington et al. 2019). Its prevalence is increasing globally with every passing year, but still many of the countries, including both developed as well as underdeveloped, lack proper disease control programmes. It has been reported from many countries of Africa, but these countries don't have sufficient information regarding its control and prevention. The reasons behind this might be lack of awareness in public as well as the lack of concern shown by respective governmental bodies. Ultimately, many of the positive cases go unreported (Whittington et al. 2019). Ruminants are the most commonly affected animal species, but it can also affect non-ruminant wildlife species (Collins 2003).

John's disease is much problematic due to its chronic nature and lack of accurate treatment till date. An infected animal is considered primary source of its transmission. Newly borne animal are at higher risk of getting infection due to their weak immune system while fecal-oral route being the most common route of its transmission (Sweeney 2011). By the time, clinical symptoms of disease in animal become noticeable to the farmer, if clinical stage of disease has already reached. It is also thought that when a single positive case is identified in herd, almost 4-8 asymptomatic carriers might have developed, in subclinical form of disease, continuously shedding the bacteria in milk and faeces. This characteristic of disease is veiled danger for the farmer. Despite the exposure to infection at early stage of life, it takes years to exhibit clinical symptoms, and in the meanwhile the infected animal will continuously contaminate the environment of farm putting all the healthy animals at higher risk (Tanaka et al. 2005).

While paratuberculosis has been extensively studied in animals, there is growing evidence suggesting its potential as a zoonotic disease, meaning it can be transmitted from animals to humans (Hovde and Moum 2012). Crohn's disease (CD) is a cataclysmic, chronic and granuloma forming disease of humans affecting their large intestine particularly ileum and colon. This is why it is also known as Crohn's ileitis as well as Crohn's Colitis and regional ileitis (Windsor 2014). According to a report, 0.8 million people in North America are affected by it annually. Its clinical signs and pathological lesions are almost similar to Johne's disease in animals but still their relationship is dubious. Various factors are responsible for the onset of this disease including genetic factors, environmental factors, and impulsive immune response (Uzoigwe et al. 2007). This chapter aims to explore the epidemiology, pathogen biology, host range & transmission, clinical

manifestations, diagnostic challenges, and prevention and control measures of paratuberculosis as a potential zoonosis.

2. EPIDEMIOLOGY

Paratuberculosis has been reported worldwide, with varying prevalence rates in different regions. It is most commonly found in countries with intensive livestock production systems, such as the United States, Europe, Australia, and New Zealand (Windsor 2014). The prevalence of this disease has been reported to increase from 21.6% to 91% in dairy herds of USA just within the period of 10 years (1996-2007). Another report estimates that almost 40% of dairy herds in USA are affected with MAP causing annual losses of more than 1.5 billion dollars to the dairy industry. Most common route of transmission is feco-oral route however the transmission may also occur via other ways like consumption of contaminated milk, vertically from infected sire to dam or from infected dam to fetus. The organism can survive in the body of host for years without causing clinical signs while host keeps shedding the organism in body secretions acting as a silent killer. This organism can survive in the environment either in its normal form (cell wall containing form) or become dormant and survive in vegetative form or gets modified into spore like form. It may even survive pasteurization thus making the milk potential source of transmission to human beings (Uzoigwe et al. 2007).

CD is prevalent worldwide. Its reported prevalence in Canada is found to be 161-319 cases per 100,000 populations. In North America, it is reported to affect 0.4-0.6 million people, while the incidence rate is found to be 6 per 100,000 people every year that is almost equal to Europe. According to reports, it is becoming more common problem in developed parts of the world. Its onset can occur at any age but the most commonly affected age group is 15-30 years (Hovde and Moum 2012). Another study revealed that the people in closed contact with the affected ones are at 3-20 times higher risk of acquiring the disease (Hovde and Moum 2012).

This disease causes significant economic losses in the agricultural industry due to decreased milk production, weight loss, and increased mortality rates in infected animals. Despite all these facts and figures, only few of the countries have proper disease control program while most of the countries don't have even research plans for control of this disease (Uzoigwe et al. 2007). However, the potential public health implications of paratuberculosis have only recently gained attention. Exact burden in humans is still unknown due to lack of awareness in general public, insufficient research funding and under reporting.

2.1. PATHOGEN BIOLOGY

MAP belongs to group known as Mycobacterium avium intracellular complex (MAIC). The majority of its strains differ from other mycobacteria as it requires an iron chelating molecule, mycobactin, from outside sources for its multiplication (Tortoli 2003). It multiplies within macrophages, interrupting the phagocytosis. In its defense, body further attempts to kill the pathogen that ultimately results in granuloma formation. This organism prefers to multiply in cells having abundant iron, pyruvate and calcium in them (De Juan et al. 2006). These bacteria have mycolic acid in their cell wall and are acid fast bacteria due to which they can't be stained via gram staining method and require specific 'acid fast

staining' method (Tortoli 2003). The presence of this substance in cell wall also makes it very difficult to break the wall interrupting the release of DNA required for conducting laboratory tests. Microscopic identification of MAP from human tissue is almost impossible. However, culture method and molecular techniques like PCR can be used for its identification. It survives within human tissue cells and in the form of spheroplast that is cell wall deficient form, due to which it can't attain Ziehl-Neelsen (ZN) stain (Chiodini et al. 1986). Therefore, its confirmation by standard light microscopy using ZN staining method becomes almost impossible. Culture growth of MAP is sluggish taking more than 3 months just for its colonies to appear while culture of samples taken from human may take more time, even a year or more to get its colonies appear.

As it has the ability to go into dormant phase, it survives for years in the environment (Whittington et al. 2004). In addition to this, humidity and acidic soil supports its survival in the environment. Therefore, it is suggested to add lime to soil of farm and its premises before introducing healthy animals. Being a meticulous creature, it requires special media for its growth on which it grows very slowly even for one year to get primary isolation.

2.2. HOST RANGE AND MODES OF TRANSMISSION

Wide range of animal species is reported to be infected with this organism including both the domestic as well as wild animals, and this host range may also extend further. MAP has been isolated from humans suffering from Crohn's disease, AIDs, and other immuno-compromising diseases, indicating its zoonotic significance (Tortoli 2003). Highest number of cases has been reported from Europe, America and Asia that may be probably due to the inadequate reporting system in other regions. The exact route of transmission of MAP to humans remains uncertain, but several potential pathways have been proposed. Direct contact with infected animals, ingestion of contaminated food or water, and inhalation of contaminated dust or aerosols are considered the main routes of transmission (Chiodini et al. 1986). Young animals particularly calves are considered to be at higher risk of acquiring infection probably due to their open gut, presence of Peyer's patches; a specialized lymphoid tissue, believed to accept maternal antibodies. The infection due to MAP is dose dependent; thereby aged animals are susceptible to infection with higher dose. Along with this, onset of disease is also affected by the dose; higher the dose, speedier will be the onset of disease (Weber et al. 2010). Additionally, consumption of unpasteurized milk and dairy products derived from infected animals has been suggested as a potential source of human infection. Regardless of the route of entry, host's intestinal tissue acts as a suitable habitat for this organism. Once entered into enterocytes, the dendritic cells or macrophages carry it to the nearby lymph nodes where it suppresses genes to bypass intestinal barriers. Along with this, it also decreases or quits the immune response against it.

The organism is shed in the faeces of infected animal thereby acting as a continuous source of contamination in the environment. The infected cattle are classified on the basis of the quantity of pathogen being shed in faeces. The quantity is less than 300 CFU per gram in light shedders, 300 to 3000 CFU per gram faeces in moderate shedders while heavy shedders, shed more than 3000 CFU per gram. Another type has been added named as super shedders who can shed more than 10000 CFU per gram. The contaminated pastures can also contaminate the rivers when water efflux into river due

to rainfall acting as a potential threat for both humans and animals (Pickup et al. 2006). The ability of MAP to survive in the environment for extended periods further complicates the transmission dynamics of this bacterium.

2.3. STAGES OF PARATUBERCULOSIS

Tiwari and his fellows in 2006, suggested that MAP infection has 4 phases; silent, subclinical, clinical and advanced clinical. During the first 2 stages, no clinical signs appear in infected animal due to which these 2 has been considered one in the recent classification of disease. Detail of all 4 states is as following: In silent stage, neither the infected animal shed pathogen nor is the development of detectable immune response so at this stage, pathogen detection can only be done via PCR, tissue culture or histopathology (Whittington et al. 2019). During the subclinical stage, diagnosis can be done via different tests used for pathogen detection but discontinuous pathogen shedding, that also in low quantity, leads to higher probability of getting false negative results and there is significant decrease in milk production during this stage. In the clinical stage of disease, feed intake of animal is normal or even increased but its body condition goes down, and also suffers from diarrhoea. At this stage, immune response detecting diagnostic tests are considered to be trustworthy. Emaciated animal with shooting diarrhoea is the clinical manifestation of entering the final stage of disease; the advanced clinical stage. There is development of condition called 'bottle jaw' due to decreased oncotic pressure as a result of severe protein loss (Tiwari et al. 2006).
Paratuberculosis can be explained very well by 'iceberg phenomenon'; which state that for a single advanced clinical case, there must be 1-2 clinical cases, 4-8 subclinical cases while 10-14 silent stage cases. Shedding of pathogen has been described by in 2 ways; Progressive and non-progressive. In the non-progressive shedding pattern, there is irregular shedding and in low number while in progressive shedding, infected animal shed pathogen continuously, in too large number (Behr et al. 2020).

3. ZOONOTIC POTENTIAL OF PARATUBERCULOSIS

A worldwide movement called one health approach is addressing the impact of zoonotic diseases occurring at animal, human, & environment interface (Vandersmissen and Welburn 2014). One health integrated approach got recognition in 2010 as an agreement among World Health Organization (WHO), World Organization for Animal Health (OIE), and Food and Agriculture Organization (FAO) to ''cope up with health risk issues occurring at the human-animal-environment-interface'' (FAO–OIE–WHO2021). Some Zoonotic diseases got significant attention from the international community while other zoonotic diseases which are less common were not given due attention. The WHO designated these diseases as neglected zoonotic diseases (NZD), one of them is MAP or Johne's disease. The contribution of Johne's disease zoonosis to Crohn's disease has not been established authentically, and needs to be confirmed because it is still controversial. Moreover, MAP is now associated with many inflammatory and autoimmune diseases of humans i.e., granuloma formation in Crohn's disease, Sarcoidosis Blau syndrome, autoimmune type 1 diabetes (T1D), multiple sclerosis autoimmune thyroiditis, lupus, rheumatoid arthritis and possibly, Sjogren's syndrome

(Cossu et al. 2017; Ekundayo et al. 2022). The causal linkage of following diseases with MAP is further elaborated: Crohn's Disease, rheumatoid arthritis, T1D, multiple sclerosis.

3.1. MAP & CROHN'S DISEASE

The chronic granulomatous inflammation of intestines of human beings is called Crohn's disease; MAP was hypothesized to be the causative agent of Crohn's disease back in 1913 when clinical symptoms and post-mortem lesions of this disease in human were found similar to Johne's disease in cattle. CD is believed to have multiple etiological factors like genetic susceptibility, environmental factors (life style, pathogen etc.), and each playing particular role in causing disease. Initially many viruses and bacteria were supposed to be the possible cause, but later on an association between the Paratuberculosis caused by Mycobacterium avium subspecies Paratuberculosis and Crohn disease was established when Thomas K. Daziel, a surgeon in 1901 while operating a patient with chronic inflammation of the intestine observed lesions similar to that of Johne's disease, he was already aware of (Daziel et al. 1913). He collected data from other cases and published his findings in the British Journal in 1913 summarizing that the histological findings of the Crohn's disease in human were similar to that of Johne's disease (Para tuberculosis) in animals caused by MAP, thus suggesting that the disease may be the same. Few other studies have also suggested that four out of six criteria for disease's etiology have been met by MAP in relation to CD. Various studies also suggested the link of MAP with Idiopathic Bowel Disease (IIBD) that includes CD and Ulcerative colitis (UC). The association was confirmed later on when MAP was isolated from Crohn's disease patients in Australia, United States, The Netherlands, and France. The three groups of scientists working with the culture of M. Paratuberculosis isolated MAP from 20, 33, & 38% of humans suffering from Crohn's disease. Only 0.8% (1 in 121) MAP was isolated from healthy humans kept as controls. These isolates were of bovine origin as were found genetically similar to strains isolated from cattle. Confirmation of MAP as the causative agent of IIBD is still controversial but once it is confirmed, it would be a major public health issue in the years to come. Approximately 1-2 million people, across the globe, are believed to be affected by CD. Paratuberculosis in humans, also known as human paratuberculosis or Crohn's disease, shares certain clinical similarities with Crohn's disease, a type of inflammatory bowel disease (IBD). Chronic diarrhoea, visceral sensitization, fatigue, weight loss, and fever are the major symptoms. However, the diagnostic criteria for human paratuberculosis are not well-established, leading to challenges in accurately diagnosing and differentiating it from other gastrointestinal disorders. Further research is needed to establish a clear link between MAP infection and human Paratuberculosis (Grant 2005).

3.2. MAP AND TYPE 1 DIABETES MELLITUS

A chronic autoimmune disease known as type 1 Diabetes (T1D) is related with cow milk exposer in early life. To check the association of cow milk with T1D a study was conducted in 15 countries at various 78 centers and it was established that Mycobacterium avium subsp. paratuberculosis present in the milk triggers the disease, thus establishing a latent MAP infection in infants due to shared genomic risk for both mycobacterial infections and T1D. Further it was studied that MAP's immunodominant heat shock protein 65 (HSP65)

cross reacts with glutamic acid decarboxylase (GAD) of pancreatic origin due to its molecular mimicry resulting in the production of anti-GAD antibodies which cause the immune mediated destruction of pancreatic cells which produce insulin. It was also postulated that MAP may also serve as environmental trigger for T1D in the population genetically at risk, the same was supported by three proposals: shared genetic susceptibilities between mycobacterial infection and T1D, epitopic homologies of pancreatic glutamic acid decarboxylase and HSP65 protein of MAP, and epidemiological correlation with the early age exposure to cow milk. Later on, Sechi and associates on the island of Sardinia which has second highest incidence of T1D in the world also established relationship between T1D and MAP. Map was reported only in T1D patients and not in T2D patients (Sechi et al. 2008). Additionally, MAP peptides homologues to pancreatic proteins were also identified and proved that immune response to these MAP peptides cross react with the classical islet cell antibodies (Niegowska et al. 2016). More than a dozen studies published in various articles implicated MAP in T1D, whereas only one article of Indian origin stated that MAP could not be found in the blood of T1D patient. Interestingly by BCG vaccination of T1D individuals, followed by a booster dose after one month interval, blood sugar level was controlled as BCG provides cross protection against Paratuberculosis. The normal blood sugars level was observed up to eight years after the vaccination (Ku¨htreiber and Faustman 2019). It has been further established that BCG vaccination is quite effective against MAP as it is effective against tuberculosis and non-tuberculosis bacteria (Dow 2018).

3.3. MAP AND MULTIPLE SCLEROSIS

The link between MAP and multiple sclerosis (MS) has been found in various studies in Italy. Similarly in Japan it has been observed that MAP is the risk factor or the microbial trigger of the MS in patients having genetic susceptibility to mycobacterium. Various other studies have also linked MAP along with other microbial triggers of multiple sclerosis in the populations of Italy and Japan (Ekundayo et al. 2022). Anti-myelin basic protein is used to detect Antigenic peptides of MAP and Epstein-Barr virus (EBV) in MS individuals (Mameli et al. 2014). On the other side, spinal fluid of MS individuals was found positive for anti-MAP antibodies (Yokoyama et al. 2018). In 2022 a significant media response was seen when the issue of a journal science published a report revealing the prevalence of multiple sclerosis in association with EPV on the basis of large database (Bjornevik et al. 2022). However, even based on huge data, the revealing was not novel as already it was established that EBV, MAP and human endogenous retroviruses (HERVs) are the microbial triggering agents of the multiple sclerosis (Frau et al. 2021).

3.4. MAP AND RHEUMATOID ARTHRITIS

The uptake and onward survival of MAP in the human cells is favored by the cholesterol enrichment and MAP has the ability to manipulate lipid metabolism process of the host and accumulate cholesterol in the macrophages to enhance infection just like other pathogenic mycobacteria (Johansen et al. 2019). This sort of relationship between host cholesterol level and reaction of MAP is observed in rheumatoid arthritis (RA) along with other diseases like autoimmune diabetes and multiple sclerosis. MAP has been associated with RA as tyrosine phosphatase A (PtpA) and kinase G (PknG) the virulence

factors of MAP necessary for its survival in macrophages are significantly found in RA patients supporting the hypothesis that MAP is involved in the RA pathogenesis. Clinically RA is referring to erosive damage of joints along with cellular and humoral responses to various self-peptides like Interferon regulatory factor 5 (IRF5). The MAP_4027 antigen of MAP also targets IRF5 thus supporting the hypothesis that MAP infections trigger a self-peptide of RA immune response and which involve in disease pathogenesis (Bo et al. 2018). A recent study also established the possible role of many microbial antigens in the triggering and pathogenesis of various diseases. All the studied antigens showed humoral response in RA patients as compared to controls (Jasemi et al. 2021). HERVs are also linked with many autoimmune diseases (Balada et al. 2010).

4. TRANSMISSION OF MAP FROM CATTLE TO HUMANS

4.1. MAP IN THE ENVIRONMENT

MAP is a very resilient microorganism and survives in soil and water up to 120 weeks after its shedding by the infected animals in the environment (Garvey 2020). Map has been detected in grazing areas as well as in runoff water continuing to rivers and municipal waters. These water sources serve as reservoir of MAP as it survives in the biofilm (Botsaris et al. 2016). The efficiency of chlorination or sand filtration methods to inactivate or remove MAP from contaminated water has not been fully investigated. There is only a little information available regarding the effect of chlorination on MAP present in water destined for human's consumption according to which it can only reduce two $\log^{10}$ the numbers of viable MAP in contaminated water (Whan et al. 2001). Cattle manure in different forms is used as fertilizer to agricultural land thus heavily contaminating the grass if the manure is from MAP infected animals. MAP persists on depopulated farms and in the roots & aerial parts of the plants of the pasture plots contaminated with MAP (Kaevska et al. 2014). MAP is also found in aerosol form and inhalation is another possible transmission route of MAP to animals and humans (Rhodes et al. 2014). Due to the inadequacy of MAP diagnostic testing along with latent nature of infection in apparently healthy animals, the farmers are reluctant for the routine testing which result in continuous MAP shedding in the environment, trade of asymptomatically MAP infected animals and delayed culling of infected thus contaminating the environment with MAP (Garvey 2020).

4.2. MAP IN FOOD

Mycobacterium can be found in various food products, like milk and beef, which ultimately act as a potential source of its transmission. Their detail is given below;

4.2.1. MILK AND DAIRY PRODUCTS

Milk and other milk products are the major source of MAP infection in humans. MAP has been detected from yogurt, cheese and muscle meat (Dow and Alvarez 2022). Map has been recovered from the milk of cows both sub-clinically and clinically infected with Johne's disease. It may also be recovered from the milk of other ruminants such as goats and sheep affected by Johne's disease. MAP enters milk directly from within the udder

or by contamination from different sources while milking. The intake of Map infected colostrum or milk is considered as major source of transmission of Johne's disease from cow to calf in an infected herd, thus it is recommended; to control the spread of the disease the calves should not be fed with map infected milk (Collins 2003). Likewise, mostly human's intake cow milk at a very young age, thus cow milk has been considered as a potential source of transmission of the MAP from cattle to humans. As mostly cow milk is pasteurized before its use, many studies have been conducted to check the efficacy of pasteurization and various pasteurization approaches regarding MAP, many of these studies depicted that MAP is more heat resistant as compared to other mycobacteria & low numbers of viable MAP survives milk pasteurization process (McDonald et al. 2003). The factors regarding the survival have not yet been fully understood and it is supposed that the presence of higher numbers of MAP in the forms of large clumps of cells in the milk may lead to the survival of some MAP during pasteurization process.

4.2.2. BEEF

Studies have revealed that Johne's disease affects both beef and dairy cattle so; meat could also be a possible source for the transmission of MAP to human beings. It has been observed that beef of old cattle used to prepare minced meat for human consumption may be a source of MAP infection (Manning 2001). In animals culled due to clinical signs of Johne's disease, MAP infection is thought to be disseminated in the animal tissues including muscles, blood and ileocecal lymph nodes (Grant 2005).

5. DIAGNOSTIC TESTS AND THEIR CHALLENGES

To identify the animal infected with MAP is necessary in order to understand and analyse the problems due to paratuberculosis. It can be done in 2 ways; 1st one is the identification of the pathogen itself that can be done by PCR or culture method, while for other way, ELISA, agar gel immunodiffusion or complement fixation tests can be used to detect immune response. Using pooled samples for diagnostic tests is recommended due to high cost of tests (Collins 2003). True prevalence of this disease is very challenging to be analyzed as there is no availability of standard diagnostic test with 100% sensitivity (Nielsen and Toft 2008). The reported sensitivity of ELISA using milk and serum samples is found to be 25-35% only while the sensitivity of culture test using faecal samples being slightly greater; 55-65%. Using milk samples within 1st 2 weeks of lactation or after 45 weeks can be a way to get ELISA results with better sensitivity (Lombard et al. 2013). Prevalence of paratuberculosis in herd can also be assessed by using environmental samples and performing their culture test or PCR. For this, it is recommended to collect samples from manure storage, particularly pooled samples, in order to get higher sensitivity as well as specificity (Lombard et al. 2013).

Hence, one of the major challenges in diagnosing paratuberculosis as a zoonotic disease is the lack of standardized and validated diagnostic tests. The current diagnostic tests used in animals, such as faecal culture and serological assays, are not suitable for human use due to their limited sensitivity and specificity. Developing accurate and reliable diagnostic methods for detecting MAP in humans is crucial for identifying infected individuals, understanding the true prevalence of human paratuberculosis, and implementing appropriate control measures.

6. PREVENTION AND CONTROL MEASURES

MAP infection is not only causing huge economic losses in dairy industry and acting as a serious public health concern, it also hinders the trade of animals as well as animal products across the borders. These three are major reasons why its control and prevention need immediate and serious attention. By the time, organism is identified in herd; significant damage has already been occurred in the form of its transmission, probably to all the nearby animals (Whittington et al. 2001). Preventing and controlling paratuberculosis in both animals and humans requires a multi-faceted approach. For animals, measures such as culling infected animals, improving herd management practices, and implementing strict biosecurity measures can help reduce the spread of MAP. In humans, promoting awareness about the potential risks associated with paratuberculosis and adopting hygienic practices, such as pasteurization of milk and dairy products, can minimize the chances of infection. Additionally, further research is needed to develop effective vaccines and therapies for both animals and humans.

7. CONCLUSION

Paratuberculosis, is primarily a disease of ruminants, also has the zoonotic potential to be transmitted to humans. Various aspects related to the epidemiology, pathogenesis, clinical manifestations, transmission & diagnostic challenges along with prevention and control measures to minimize the risk of Paratuberculosis zoonosis have been elaborated in this chapter. As the evidence linking MAP infection to human paratuberculosis is still evolving, it is essential to focus more on rendering awareness about the potential risks related with Paratuberculosis zoonosis and encourage further research and development to better understand and manage this complex disease for the benefit of both animal and human health. Continued collaboration between veterinary and human medical professionals is crucial in addressing the challenges associated with Paratuberculosis zoonosis.

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