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REVIEW ARTICLE

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Tuberculosis in Swine: Prevalence and Basic Diagnostic Approach

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ABSTRACT

Tuberculosis (TB) occurs in all vertebrates and some cold-blooded animals. It occurs worldwide and the disease in domestic species and people occurs less often than in developing countries. The causative organism, Mycobacterium tuberculosis, is subclassified into several types: human, bovine, and avian. The avian type is called M. avium (or M. avium complex) which affects mainly birds but is also found in the environment. Pigs rarely become infected with the human types (M. tuberculosis) or bovine (M. bovis) but are often infected with M. aviumcomplex. The M.avium complex also causes non-progressive, sub-clinical illnesses in healthy people. Mycobacterium avium serotypes 1, 2, 4, 5, and 8 were isolated from tissues of affected animals. These serotypes are responsible for approximately 85% of the mycobacterial infections found in swine as the reported from the United States. The epidemiology of swine tuberculosis in Ethiopia and its pathology and pathogenesis were not well studied. Even, a few articles published from Ethiopia were only targeted to the central areas of the country where some swine farms for foreigner's consumption. The low report is due to fewer consumption habits of pork in Ethiopia. Due to traditional and religious aspects that protect many peoples from eating pork, a very low production system of swine. Therefore, this minireview was designed to address the prevalence and diagnostic approach for swine tuberculosis in Ethiopia.

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Introduction

Tuberculosis is the deadly disease affecting human and animals throughout the world. It is a chronic, granulomatous disease of swine, poultry, wild birds, many domestic and wild animals and people [1]. Although many species of tuberculosis affecting different animals including humans are found, Mycobacterium avium infection is a severe condition in humans, whereas pigs are often subclinically infected2. According to Agdestein et al.2, Mycobacterium avium subsp. hominissuis was detected in samples of faeces, peat and lymph nodes from infected groups, often with identical Multi-Locus Variable Number of Tandem repeat Analysis (MLVA) profiles. Additionally, other non-tuberculous mycobacteria (NTM) were found in the same material. The absence of macroscopic lymph node lesions in the presence of M. avium subsp. hominissuis was frequently demonstrated [2].

The fragmented host and pathogen population where the main factors for transmission of tuberculosis and its environmental complexity, mainly in terms of the diversity of suitable domestic and wild Mycobacterium tuberculosis (MTC) hosts [3]. Researchers at the University of Pennsylvania, New Bolton Centre, found that the disease, called swine tuberculosis is minimally contagious in swine herds. "Swine tuberculosis has great economic impact, actually what is called swine tuberculosis is not a tuberculosis in the traditional sense. Instead, these animals have lesions caused by M. avium, an organism which causes tuberculosis in poultry and wild birds. The swine seams healthy and show no clinical signs of disease. However, when the animals are slaughtered the meat inspector finds the lesions"4. M. avium infection is swine causes lesions indistinguishable from those caused by M. tuberculosis (TB in humans) or M. bovis (TB in cattle). Swine are susceptible to all three infections and, if they contract the latter two, will often show clinical signs of disease [4].

Swine were infected with M. bovis to develop a model for pulmonary and disseminated tuberculosis in humans [5]. Tuberculosis is known by latent infection and the low tissue bacterial burden associated with tuberculous latency is a major obstacle to characterizing the mechanisms by which M. tuberculosis persists and reactivates in the host. The prevalence of tuberculosis caused by M. bovis within the Central Otago feral pig population, was estimated by the surveys undertaken in three localities, was approximately 31% [6]. Epidemiology of tuberculosis (TB) infection in swine in Argentina were reported from isolates (n = 196) obtained from TB-like lesions (n = 200) were characterized by polymerase chain reaction. The isolates were positive to either M. bovis (IS6110) (n = 160) or M. avium (IS1245) (n = 16) while the remaining 20 (10•2%) isolates were positive to both M. bovis and M. avium. The detection of both bacteria together suggests co-infection at the animal level. In addition, MAC-positive isolates (n = 36) were classified as M. avium subsp. avium (MAA) (n = 30) and M. avium subsp. hominissuis (MAH) (n = 6), which resulted in five genotypes when they were typed using mycobacterial interspersed repetitive unit, variable number of tandem repeats (MIRU-VNTR) [7].

The difficulty of latent infection is further compounded by the lack of a much-needed genuine animal model of latent tuberculosis for stringently testing the validity of putative mechanisms underlying the persistence of the tubercle bacillus. Nevertheless, based on results of in vitro experimentation, various mycobacterial

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components have been identified as candidate persistent factors that may play a role in the establishment of the latent state of infection. More important, existing animal models, particularly those of the mouse, have been employed to evaluate the significance of these mycobacterial factors in tuberculous persistence. The use of the low-dose, persistent-infection murine model for tuberculosis, despite certain limitations, has been particularly useful for elucidating the roles of various M. tuberculosis components in tuberculous persistence [8].

The other pathologic study was commenced by Whitlock veterinary pathologist at Pensuviela University explained that tuberculosis lesions caused by M. avium in swine are not infectious to humans in general, though there may be some danger to individuals with a compromised immune system. AIDS patients often have mycobacterial infections as complications of the primary disease. "On gross examination the lesions of swine TB cannot be distinguished from those caused by, for example, M. tuberculosis. Therefore caution is necessary. The meat is cooked if lesions are found in two body cavities. This, unfortunately, reduces the value of the carcass by 50 percent. If lesions are found in three body cavities, the meat is condemned, causing a total loss [2].

Epidemiology of Swine Tuberculosis

Tuberculosis (TB) occurs frequently in man, domestic and wild animals, poultry and wild birds. It occurs in almost all vertebrates and in some cold-blooded animals. This study reported in the US and the disease in domestic species and people occurs less often than in developing countries. Tuberculosis is present worldwide throughout the year and is a major cause of death around the world, with most of the 1.5 million deaths per year attributable to the disease occurring in developing countries [1, 8].

The study done in Italy of Sicily province stated that “MTC strain diversity was positively related with cattle bTB prevalence, presence of wild hosts and the number of imported cattle, but not with island size, isolation, and cattle density. The study identified three most common spoligotype patterns coincided between Sicily and mainland Italy. However in Sicily, these common patterns showed a clearer dominance than on the Italian mainland, and seven of 19 patterns (37%) found in Sicily had not been reported from continental Italy” [3] This shows that the barrier should be there for the transmission of tuberculosis even within and between species in the same country. Swine tuberculosis is rare today, but the most common is the Mycobacterium avium complex (MAC) [9].

The distribution of tuberculosis was very rapid in African continent. From a total of 21 African countries reported 1123 outbreaks of Tuberculosis to the African Union-Interafrican Bureau for Animal Resources (AU-IBAR) in 2011, which contrasts with just 15 outbreaks reported in 2010. A total of 4950 cases were reported with 3364 animals slaughtered which is again a significant increase compared to the situation in 2010. Democratic Republic of Congo (DRC) recorded the highest number of cases (1944), followed by Tunisia (1047), Malawi (391) and Cote d’Ivoire (296). Ethiopia was reported one outbreak and five cases, without any report of death, slaughter and destroying [10].

The distribution of tuberculosis is not species specific and depends also on each age categories. However, the degrees of virulence and transmission speed vary among underlying factors, species, body conditions and ages of animals. The study done in Ethiopia reported that, age and origin of pigs were significantly associated ($P<0.001$) with the prevalence. In contrast, an association of sex, floor type and water source with the prevalence were not be shown [11]. The researchers concluded that the spread of M. avium by contact is minimal. They then investigated whether the disease could be transmitted from dam to offspring. However, the interspecies transmission of the M. avium was approved by study undertaken by Serriano et al. [12].

The marked resistance of mycobacteria to environmental factors makes contaminated premises a long-term threat to swine. The TB organisms usually are spread to swine by tuberculosis-infected poultry, wild birds, cattle or people, or by soil or bedding materials contaminated by them. The other less common but proven routes of exposure include exposure to serovars of avian type contained in sawdust or wood shavings used as bedding, congenital exposure of foetuses of infected, pregnant sows, and animal-to-animal exposure among swine. Some infected swine have TB lesions in their tonsils or intestine and shed the organisms in their feces1. A review undertaken at Michigan state university and the epidemiology of BTB in Michigan cattle, privately owned cervids, and wildlife between 1975 and 2010 were undertaken and they concluded as currently used BTB eradication strategies have successfully controlled BTB spread [13].

Pathology and Pathogenesis of Swine Tuberculosis

Pigs usually become infected with M. avium by ingesting the organism with contaminated feed and/or water. After ingestion, the organism penetrates the wall of the pharynx near the tonsils or the wall of the small intestine and becomes localized in the mandibular and mesenteric lymph nodes respectively14. The complex lipid nature of the organisms may explain the difficulties that body defences have in destroying mycobacteria though phagocytosis and oxidative killing. In mononuclear phagocytes, toxic lipids in the mycobacteria, or factors released by them, appear to interfere with phagolysosome formation or to inactivate lysosomal enzymes. If macrophages fail to destroy ingested mycobacteria, they can carry them to other sites. There, the bacteria are liberated upon death of the macrophages and released organisms set up new foci of infection [1].

The oral routes pathogenesis in swine is very common than other routes of transmission and TB bacilli appear to infect the tonsils and intestinal mucosa initially and then spread to the regional lymph nodes, especially those of the cervical area, less often to mesenteric nodes. Lesions in the nodes tend to develop slowly and, in most cases, the bacilli are successfully walled off. Only occasionally does the infection generalize, usually in older breeding stock infected with M. bovis [1].

The study conducted on one hundred and twelve (120) pigs were shot in the Lindis/Dunstan endemic area. One hundred and five (105) were autopsied, of which 33 (31%) had histologically confirmed tuberculous lesions. The age of pigs shot ranged from six months to five years. Because of the nature of the country they were well distributed and could easily move from one part of the endemic area to another. Thirty-five pigs were shot in the Waitaki/Hawkdun/ Rough Ridge area. All were autopsied and nine (26%) were confirmed to have tuberculous lesions. Of the 77 histologically positive pigs, 41 (53%) were cultured for mycobacteria. Sixteen (16) successful isolations (39%) of M. bovis were made, with one additional sample being considered as producing a suspicious result. One isolation of MAC was made [6].

An experimental study undertaken at Iowa State University of America reported, pigs were inoculated with various doses of M. bovis by intravenous (iv), intratracheal (int), or tonsillar routes. Animals were euthanized between 17 and 60 days after inoculation, and tissues were collected for culture and histopathologic examination. Lesions of disseminated tuberculosis were found in pigs given 104 or 108 cfu of M. bovis iv or int; localized pulmonary disease was found in pigs given 102 or 103 cfu of M. bovis int. Lesions ranged from well-organized tubercles with coagulative necrosis, epithelioid macrophages, and fibrosis to large expansive tubercles with liquefactive necrosis and extracellular growth of M. bovis. The main findings from this study was tuberculous meningitis which was observed in animals given M. bovis iv and they concluded that swine infected with M. bovis are a useful animal model for elucidating the mechanisms of pathogenesis and host defense to tuberculosis in humans [5].

Gross pathological changes found in pigs after inoculation of M. bovis were tuberculosis granulomas in the lungs, liver, spleen, peritoneum, and multiple lymph nodes. In pigs with disseminated disease or disease localized to the thorax, lung lesions varied from diffuse consolidation to multiple discrete granulomas. Fibrinous and granulomatous pleuritis were common. As well the microscopic changes were also analysed and granulomas in the liver or hepatic or mesenteric lymph nodes, multifocal areas of coagulative necrosis surrounded by macrophages, multinucleated giant cells, and smaller numbers of lymphocytes [5].

Tuberculous meningitis is the most severe form of tuberculous infection (Mycobacterium tuberculosis) and presents as a subacute syndrome with lymphocytic pleocytosis and low glucose in the cerebrospinal fluid (CSF) and meningeal enhancement of the basal cisterns and hydrocephalus on neuroimaging15. Mortality rate of this infection remains at approximately 25% of the patients. Parenchymal involvement (tuberculomas and spinal cord damage) may also appear. Nontuberculous mycobacteria affect AIDS patients. MAC is most frequently implicated. CNS infection is rare and occurs with disseminated disease.

Transcripts belonging to latency and cell envelope biogenesis were upregulated in the intestinal tissues whereas those belonging to intracellular trafficking and secretion were upregulated inside the macrophages. Transcriptomes of natural infection and in vitro macrophage infection shared genes involved in transcription and inorganic ion transport and metabolism. Mycobacterium avium subsp. Paratuberculosis (MAP) specific genes within large sequence polymorphisms of ancestral M. avium complex were downregulated exclusively in natural infection [16].

Many studies reported the organ prevalence of tuberculosis in swine. From fifteen (15) M. bovis strains isolated from 63 wild boar samples (62 from mandibular lymph nodes and 1 from a liver specimen). Sixteen mediastinal lymph nodes of 16 head of cattle were collected, and 15 M. bovis strains were subsequently cultured [12]. All M. bovis strains showed the typical spoligotype characterized by the absence of the 39 to 43 spacers in comparison with the number in M. tuberculosis. A total of nine different clusters were identified by spoligotyping. The largest cluster included 9 strains isolated from wild boars and 11 strains isolated from cattle, thus confirming the possibility of transmission between the two animal species. Fingerprinting by RFLP analysis with the IS6110 probe showed an identical single-band pattern for 29 of 30 strains analyzed, and only 1 strain presented a five-band pattern [12].

Diagnosis of Swine Tuberculosis

The initial diagnostic method of tuberculosis was started by intradermal injection of tuberculin, adaptive for dears and applied at mid-cervical sites. The swine tuberculin testing was started and conducted on one herd during 1966 [17]. The tuberculin skin test is conducted using M. avium purified protein derivatives (PPD) injected intradermally on the dorsal surface of the ear and the site observed at 48 hours for swelling and induction [10]. The accurate identification of tuberculosis in swine as well as other animal species like cattle is crucial in test and slaughter disease control program [18]. This report also approves as accurate diagnosis will be crucial component in the control programme of tuberculosis in cattle and deer [18]. A major effort to eradicate tuberculosis in cattle, other animals and in people markedly reduced incidence of the types of tuberculosis usually seen in animals and people [1].

The report of Whitlock advocates the use of the ELISA test to determine whether swine are infected with M. avium. "This test is more accurate than the skin test. Unlike the skin test, it could provide indication that one is dealing with M. avium and not one of the more dangerous forms of mycobacterial infections [4]. Researchers found that the pigs inoculated with M. avium showed a positive reading to the skin test six weeks after the infections. The control group did not show any positive results to the skin test. Positive readings for M. avium infection in the inoculated animals occurred in the ELISA test at about eight weeks after infection. The control group, which had mingled with the infected animals, did not show positive results of the skin test nor could the ELISA test detect any antibodies to M. avium.

At postmortem, the pigs were inspected for lesions and the most severe were found in pigs that had been infected at age of eight weeks. The lesions were less serious in the animals infected at a later age. No lesions were found in the control group. The finding of large numbers of acid-fast bacteria in smears from lesions provides a tentative diagnosis [10].

The report of Barandiaran et al [7]. stated that there is co-infection of M. bovis and MAC, therefore, the isolation of bacteria should be done from granulomatous lesions; which strengthen the idea that MAC is the infective agent. The criteria used to determine co-infection were confirmation by PCR of two species in suspensions from at least two colonies grown in culture media. This study considered infection present when a single species of Mycobacteria was confirmed by PCR [19].

The most commonly and economical use of tuberculosis diagnosis in many countries of the worlds are gross pathological study, culturing, acid-fast staining and molecular diagnostic methods. Accordingly, different authors used different methodologies and diagnostic techniques for reporting tuberculosis. Arega et al [11]. reported culture positivity confirmed in 30.6% (15/49) of the tuberculous-like lesions and of the 15 isolates, 12 were acid fast positive while five of the latter were confirmed by multiplex PCR as members of the MTC. Speciation of the five isolates further confirmed that they were M. tuberculosis, belonging to

SIT1088 (two isolates) and SIT1195 (one isolate). The remaining two isolates belong to an identical spoligotype, the pattern of which was not found in the spoligotype database (SpolDB4). Polymerase chain reaction (PCR) and immunohistochemistry (IHC) are increasingly useful for confirmation [10]. Diagnosis of tuberculosis made by culture takes long time of involved tissues (growing the bacteria), a process that takes at least eight weeks and therapy requires a prolonged, multidrug regimen[15, 20]. An estimated 60 million lives were saved through TB diagnosis and treatment between 2000 and 2019. Ending the TB epidemic by 2030 is among the health targets of the United Nations Sustainable Development Goals (SDGs) [21].

Prevalence of Swine Tuberculosis in Ethiopian

Ethiopian livestock populations are out-numbered other African countries, even many countries of the world. Although swine farming has huge economic important in many developing countries, in Ethiopia it's very limited due to traditional and religious aspects that protect eating pork. For this reason, there is paucity of information in the epidemiology and pathology of tuberculosis in swine though the endemic occurrence of bovine tuberculosis was elucidated in Ethiopia [22]. Many of the farming system, depends on livestock in the country are at pastoralist areas. Pastoralism is a way of life in which food supply is produced from animals by using a variety of herding practices based on constant or partial herd mobility in the low land areas of Ethiopia [23]. Many studies were conducted on tuberculosis infection in different species of animals including human in Ethiopia. An individual animal prevalence of 2.0%, 0.4%, and 0.2% was reported in cattle, camels, and goats, respectively [23].

From reviewed literature, studies indicated the prevalence rate of BTB with a range of 3.4% (in small holder production system) to 50% (in intensive dairy productions) and a range of 3.5 to 5.2% in slaughter houses in various places of the country [24].

The prevalence of the disease is not well established in livestock and most studies focused mainly on Central Ethiopia, whereas large areas in the country remain un-investigated [25]. Arega et al. was reported 5.8% (49/841) estimated prevalence of swine tuberculosis. Before this study there were no reported prevalence of swine tuberculosis in Ethiopia and they were designed to estimate the prevalence of TB in pigs in central Ethiopia and characterized the causative agents [11]. Shiferaw et al [26]. reported, 19.6% (109/556) prevalence of swine tuberculosis, out of five hundred and fifty six (556) swine examined, tubercle like granulomatous lesion were detected in different organs. The same studies conducted in different areas of the country were also reported. Of the total 329 heads of swine tuberculin tested by bovine purified protein derivative antigen, an animal level prevalence of 3% (95% CI: 2-6) and a herd level prevalence of 11% (95% CI: 1-49) were observed at a cut-off value of >2mm22. The systematic review done by Sebhat et al [27]. were reported 5.8% (95% CI: 4.5, 7.5) pooled prevalence of bovine tuberculosis in Ethiopia.

Conclusion and Future Direction for Diagnosis of Swine Tuberculosis

The isolation of M. tuberculosis from pigs suggests a possible risk of transmission between humans and pigs. Setting norms and standards on TB prevention and care and promoting and facilitating their implementation; Developing and promoting ethical and evidence-based policy options for TB prevention and care; Ensuring the provision of specialized technical support to Member States and partners jointly with WHO regional and country offices, catalysing change, and building sustainable capacity; Monitoring and reporting on the status of the TB epidemic and progress in financing and implementation of the response at global, regional and country levels are among the strategic issues to be undertaken for control and prevention of tuberculosis from this world. Globally, TB incidence is falling at about 2% per year and between 2015 and 2019 the cumulative reduction was 9%. This was less than half way to the End TB Strategy milestone (ETSM) of 20% reduction between 2015 and 2020. According to the WHO report, an estimated 60 million lives were saved through TB diagnosis and treatment between 2000 and 2019. Ending the TB epidemic by 2030 is among the health targets of the United Nations Sustainable Development Goals (SDGs). Hence, establishing feasible control methods is required and the future strategic planning on the study of swine tuberculosis and economic benefits of swine industry in developing countries, particularly in Ethiopia should be engaged.

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