



Review Article

AYURVEDIC INSIGHTS INTO RE-EMERGING HUMAN BRUCELLOSIS

Krishna G S^{1*}, L Mahadevan², Kasthuri Nair A³, Arun Pratap⁴

*¹PG Scholar, ²Professor, ³Assistant Professor, ⁴Professor & HOD, Department of Kayachikitsa, Pankajakasthuri Ayurveda Medical College & PG Centre, Kattakada, Thiruvananthapuram, Kerala, India.

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ABSTRACT

Brucellosis is a bacterial infection caused by *Brucella melintensis*. It is one of the most widespread endemic zoonotic diseases present globally, more prevalent in developing countries. It is transmitted to humans either through direct contact with infected animal tissues or fluids or indirectly by ingesting contaminated meat and unpasteurized dairy products. The route of transmission includes mainly mucocutaneous. Farmers, butchers, hunters, and veterinarians are mainly at higher risk of contracting this condition. Mostly the affected individuals exhibit flu-like symptoms, remittent fever, malaise, arthralgia, and weight loss which lasts from a few days to several years. The condition is often misdiagnosed due to nonspecific clinical symptoms, leading to inadequate treatment and prolonged illness leading to severe complications like endocarditis. Currently, there is no vaccine for human brucellosis. The modern management includes administration of antibiotics. The gold standard diagnostic tool is direct bacteriological testing. Ayurvedic understanding of endemic diseases highlights the unique concept of *Janapathhodhwamsa* proposed by *Acharyas*. They considered *Vayu*, *Jala*, *Kala*, and *Desa* as common factors in manifestation of disease. Any alteration in these factors can be understood as imbalance and disease outbreak emerged due to urbanization, lack of hygienic measures in animal husbandry, etc. remaining a public health hazard. Brucellosis is known by its undulant nature which closely resembles the *Vishama Jwara* in classics which is a *Sannipatika* type of *Jwara*. *Amapachana*, *Shodhana*, and *Samana* line of management followed by *Rasayana*, *Satvritta Palana* as a preventive line can be adopted to manage Brucellosis.

INTRODUCTION

Brucellosis is a typical bacterial zoonoses recognized as a world health problem caused by a group of bacteria belonging to the genus *Brucella*. The organism was first isolated from the human spleen of fatal cases in Malta in 1887^[1]. Brucellosis has a worldwide distribution, more prevalent in developing countries. The true global prevalence of human brucellosis is unknown because of the imprecision of diagnosis thus many cases remain undiagnosed. This typical bacterial infection is transmitted directly or indirectly to humans from infected animals, predominantly domesticated ruminants (cattle, sheep, goat), dogs, and swine^[2].

The bacilli exist in six biological variants in preferred hosts and four species have pathogenicity in humans. Among them, *B.melitensis*, small gram-negative, non-motile coccobacilli acquired from sheep, goats, and camels is the most pathogenic and the most common cause of symptomatic disease in humans^[3]. The infected animal excretes brucella in the urine, milk, placenta, and discharges. Humans usually acquire this infection on occupational exposure and thus the related risk group due to close contact includes farmers, butchers, veterinarians, and laboratory personnel, as well as travellers.^[4]

The modes of transmission to humans include- (a) Contact infection, by direct contact with infected blood, urine, placenta, and vaginal discharge, penetration through abraded skin, mucous, or conjunctiva, and inhalation. (b) Indirectly by ingesting contaminated meat and unpasteurized dairy products. Person-to-person transmission is extremely rare. Expansion of animal industries and urbanization, lack of hygienic measures in animal husbandry, and food

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handling lead to public health hazards.^[5] Overcrowding of herds, high rainfall, limited exposure to sunlight, and unhygienic practices in milk and meat production are some of the factors that contribute to favorable conditions for the spread of infection. The organism can survive for weeks, or months in favorable environments. The pathogen is killed by boiling at 60°C and pasteurization. The incubation period is 1-4 weeks but may be as long as 6 months or more ^[6]. Brucellosis in humans commonly presents a variety of non-specific clinical signs including acute fever, profuse sweating, malaise, fatigue, and arthritis, and chronicity and recurring nature with joint pain as common sequelae.^[7] Ayurvedic understanding of endemic diseases highlights the unique concept of *Janapathhodhwamsa* proposed by *Acharyas*. Brucellosis is known by its undulant nature which closely resembles the *Vishama Jwara* in classics which is a *Sannipatika* type of *Jwara*. *Amapachana*, *Shodhana*, and *Samana* line of management followed by *Rasayana*, *Satvritta Palana* as a preventive line can be adopted in the management of Brucellosis

Brucellosis in Humans

Pathogenesis

After the entry of the organism, it quickly enters lymphatics, travels through the regional lymph nodes, leading to their enlargement^[8]. Thereafter they enter the bloodstream (hematogenous spread) with ultimate localization in the reticuloendothelial system (RES). Upon entry into the tissue, cytokines such as Interleukin (IL) 12 promote production of interferon, which drives TH1-type responses and stimulates macrophage activation for phagocytosis to clear infection. 15-30% of brucella survives due to the ability of virulent *Brucella* cells to suppress TNF-alpha and will remain within the phagocytes, then it is released into circulation^[9]. Organisms inhibit apoptosis and persist within the tissues, establishing persistent intracellular infections. They proliferate in R.E cells, preferentially in bone marrow, spleen, liver, and lymph nodes where hyperplasia of R.E cells and formation of miliary granulomas occurs. The chronic localization of infection occurs at almost any site, although the RE system, musculoskeletal tissue, and genitourinary system are most frequently involved where chronic ulcerations and subcutaneous abscesses may also develop.

Clinical Features

Symptoms are variable and range from an acute febrile disease to a chronic low-grade ill-defined disease, lasting for several days, months, or occasionally. It is also known as undulant fever due to its remittent character.^[10] The common features are fever associated with profuse sweating, migrating arthralgia, and myalgia^[11]. Granuloma without caseation is the characteristic skin lesion. Onset may

be sudden or insidious, followed by an evening rise in temperature. As the disease progresses, the temperature rises to 40°C - 41°C, then subsides gradually to normal or near-normal with profuse sweating in the morning.^[12]

Initially, features like fever, chills, headache, weakness, myalgia, night sweats, arthralgia usually large joints, and insomnia are involved. In the later stages features like chronic fatigue, depression, and systemic manifestations such as cardiovascular (endocarditis), skeletal (osteomyelitis, septic arthritis), blood (hemolytic anemia, purpura), CNS (meningitis, encephalitis), optic (keratitis, optic neuritis), genitourinary (erectile dysfunction) and RES (lymphadenopathy, hepatosplenomegaly) may occur. Neurological complications (neuro brucellosis) include meningitis, meningoencephalitis, etc.^[13] The pattern of fever is continuous or remittent with daily fluctuations of body temperature like a wave/undulant but not touching normal. The onset of fever and other symptoms may be abrupt or insidious. Relapse occurs in 30% of poorly compliant patients.

Diagnosis

The clinical presentations are variable for early diagnosis so a diagnostic clue in the patient's history is necessary. Diagnosis is established in cultures of blood, bone marrow, exudates, and biopsy specimens during the acute phase of the disease and by the serological tests. The gold standard tool is direct bacteriologic and serologic tests which include routine biochemical assay and PCR.^[14]

Treatment

Conventional modern management includes combined antibiotic therapy with streptomycin, Doxycycline, Rifampicin, and tetracyclines. However, relapses are common, since it is difficult to eradicate the intracellular organisms. The most rational approach for preventing human brucellosis is the control and eradication of the infection from animal reservoirs and certain protective measures to prevent direct contact with infected animals while handling livestock and vaccinating animals.

Ayurvedic Perspective

Ayurveda considers endemic diseases as an imbalance of environmental factors like *Vayu*, *Jala*, *Kala*, and *Desa*, called as *Janapathodhwamsa*, described by *Acharya Charaka*. He mentions the root cause of *Janaapathodhwamsa* as *Adharma* due to *Asatmyendriyarthasamyoga*, *Pragyaparadha* and *Parinama*^[15]. *Adharma* leads to *Bhutasanghata* or contamination. *Acharya Susruta* mentions these diseases under *Aupasargika Roga*, due to their *Samkrama* nature and also named as '*Maraka*'^[16]. *Dalhana* explains *Adharma* as the cause of *Maraka*. These Ayurvedic perspectives on communicable diseases can be applied to understand the

urbanization, expansion of animal industries, lack of hygienic measures in animal husbandry and in food handling, etc. in the emergence of Brucellosis outbreak. In Ayurveda, diseases resulting from exogenous factors are classified as *Agantuja Vyadhi*, which is of various types and one of them being *Abhishangaja*. *Abhishangaja Vyadhi* is manifested due to the influence of *Bhuta* or microorganisms and is recognized as a significant cause of communicable diseases.

As the etiology is being an exogenous factor, this endemic condition can be categorized under *Aganthuja Jwara* particularly of an *Abhishangaja*. After the entry of *Aganthu* factor, *Bhuta* i.e., pathogen, *Jwara* is manifested directly without any transitional duration and later gets associated with *Doshas*, forming *Sama Dosh*. The vitiated *Doshas* manifests *Nija Vyadhi*. In *Abhishangaja Jwara* particularly causes vitiation of *Pitta Pradhana Tridosha*, initiating inflammatory changes in the body. Based on the strength of *Tulya Dushyas* with the indulgence of *Apathya Ahara Vihara* the pattern of *Jwara* can be continuous or remittent shows *Vishamata* (irregularity).

The remittent pattern of Brucellosis can be compared with this unique *Vishamata* which can be seen in the pattern of *Vishama Jwara* where the *Sama Doshas* gets into *Leena Avastha* within the *Dhatu*. These *Sama Doshas* (pathogenic toxin or *Ama*) localizes in *Rasadi Dhatus* and *Sthanas* of respective vitiated *Doshas*, remain dormant and exacerbate under favorable environment i.e., weakness of opposing factors/ immunity. The undulant pattern, progressive spread of endotoxin and pathogenesis of Brucellosis can be correlated with the pattern and pathogenesis of *Samtata Jwara*^[17] due to the acuteness of the condition. The affliction of *Rasavaha Srotas* and the acute manifestation of *Jwara* in *Samtata Jwara* can be correlated with the lymphatic spread of endotoxins and acute febrile illness. Variation in the persistence of *Samtata Jwara* depends on the predominance of *Doshas* i.e., 7, 10, or 12 days corresponding to predominance of *Vata*, *Pitta* and *Kapha* respectively as mentioned in classics.

When the *Dosha* becomes strong and the patient is weak, the *Sama Doshas* gets localized into deeper *Dhatu* in *Leena Avastha*. A similar pathogenesis is observed in the chronic stage of Brucellosis and reemerges on suitable *Kala*, *Prakruti* and *Dushya*. When Brucellosis remains undiagnosed, this latency promotes the metabolic changes within the *Dhatu* i.e., *Dhatu Paka* which is prime factor leading to the relapse and manifestation of complications. The systemic involvement of Brucellosis closely resembles with the features of *Dhatugata Jwara*, as the pathogenicity of Brucellosis is intracellular localization

of brucella endotoxin which can be compared with the manifestation of subsequent *Dhatu* progressively.

When *Doshas* are localized in *Rasa Dhatu* the features like *Angamarda*, *Dainyam*, *Sadanam* and *Bahitapa* can be compared with features in brucellosis such as myalgia, apathy, fatigue and raised temperature respectively. Also, *Rasapradoshaja* features can be compared with features in initial stages like anorexia, loss of appetite, fever with fatigue in Brucellosis. The cutaneous manifestations of Brucella can be compared with *Raktagata Jwara Lakshana* such as *Raga*, *Pidaka*, etc. Malaise and fatigue indicate the involvement of *Mamsa Dhatu*. The typical manifestation Granuloma resembles the features of *Mamsa Pradosha* feature. Profuse sweating in the condition may be interpreted as affliction of *Medo Dhatu*. The *Rasa*, *Rakta*, *Mamsa* and *Medo Dhatu* is considered as *Sadhya*. Thus, based on the clinical features, the involvement of *Dhatu* can be understood and respective management can be adopted.

The *Dosha Paripakva* within the *Dhatu* subsides the condition but due to *Apachara* like exposure to pathogenic environment, intake of *Abhishyandi Ahara*, etc. or non-elimination of *Doshas* properly results in the relapse of *Jwara*. This shows the nature of *Punaravrtthaka Jwara* with complications. The complications of Brucellosis, such as Osteomyelitis indicates the involvement of *Asthi Dhatu* and Neurobrucellosis with features of meningoencephalitis indicating the affliction of *Majja Dhatu* which are *Krichra Sadhya*. Erectile dysfunction may indicate the affliction of *Sukra Dhatu* which is considered *Asadhya*.

Ayurvedic treatment approaches can be directed to correcting *Jataragni* and *Dhatwagni*, *Ama Pachana*, mitigate *Sama Avastha*, accelerate *Doshapaka*, improve *Dhatu Sara* and enhance *Ojas*. As it a *Kapha Pitta Pradhan Sannipatika Jwara*, *Kapha Pitta Shamana Chikitsa* can be adopted, The deranged metabolism taking place within body is the real cause of progression disease. In the acute stage, *Sama Jwara* with *Kapha Pitta* aggravation is present and, in this stage, *Langhana* can be adopted to reduce the *Kleda*. The treatment that can break the *Samprapti* at *Dhatu* level and that which improve *Vyadhikshamatva/Bala* can be adopted. In the chronic stage medicated *Ghrita* which is *Vata Pitta Samana* by its *Snighda Sheeta Guna* can be suggested.

Ayurvedic formulations with antibacterial, antipyretic, anti-inflammatory, immunomodulatory properties can be considered beneficial. *Shodhana* line of management can be adopted to eliminate the *Leena Avastha* of *Doshas* to prevent complications. *Rasayana* which are immunomodulators include *Guduchi*, *Aswagandha*, *Shatavari*, *Amalaka*, *Yashtimadhu*, etc. Also, *Acharyas* have recommended the maintenance of body by means of medicinal herbs collected before the

onset of epidemic. Following *Sadhvritta Anuvritti*, *Dharma*, *Satvika* and *Achara Rasayana* as a means of prevention.

CONCLUSION

Brucellosis is a widespread endemic condition with mild to moderate pathogenicity. The non specificity in the clinical signs and symptoms leads to misdiagnosis and delayed diagnosis leading to long-standing pathogenicity and complications. In Ayurvedic, the disease human brucellosis with peculiar undulating feature can be understood from the perspective of *Vishama Jwara* with *Kapha Pitta Pradhana Sannipatika* vitiation progressively involving all the *Dhatu*s in chronic episodes and as complications. The different clinical manifestations which are specific to each *Dhatu* are vividly described in the context of *Dhatugata Jwara*. It is a condition with least mortality. Early diagnosis and management in the initial stages can improve the quality of life of patient. The condition can be prevented from relapsing or re-emerging with appropriate preventive measures.

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*Address for correspondence

Dr. Krishna G S

PG Scholar,

Department of Kayachikitsa,

Pankajakasthuri Ayurveda

Medical College & PG Centre,

Thiruvananthapuram, Kerala.

Email:

dockrishnags310@gmail.com

Ph: 9074051306

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