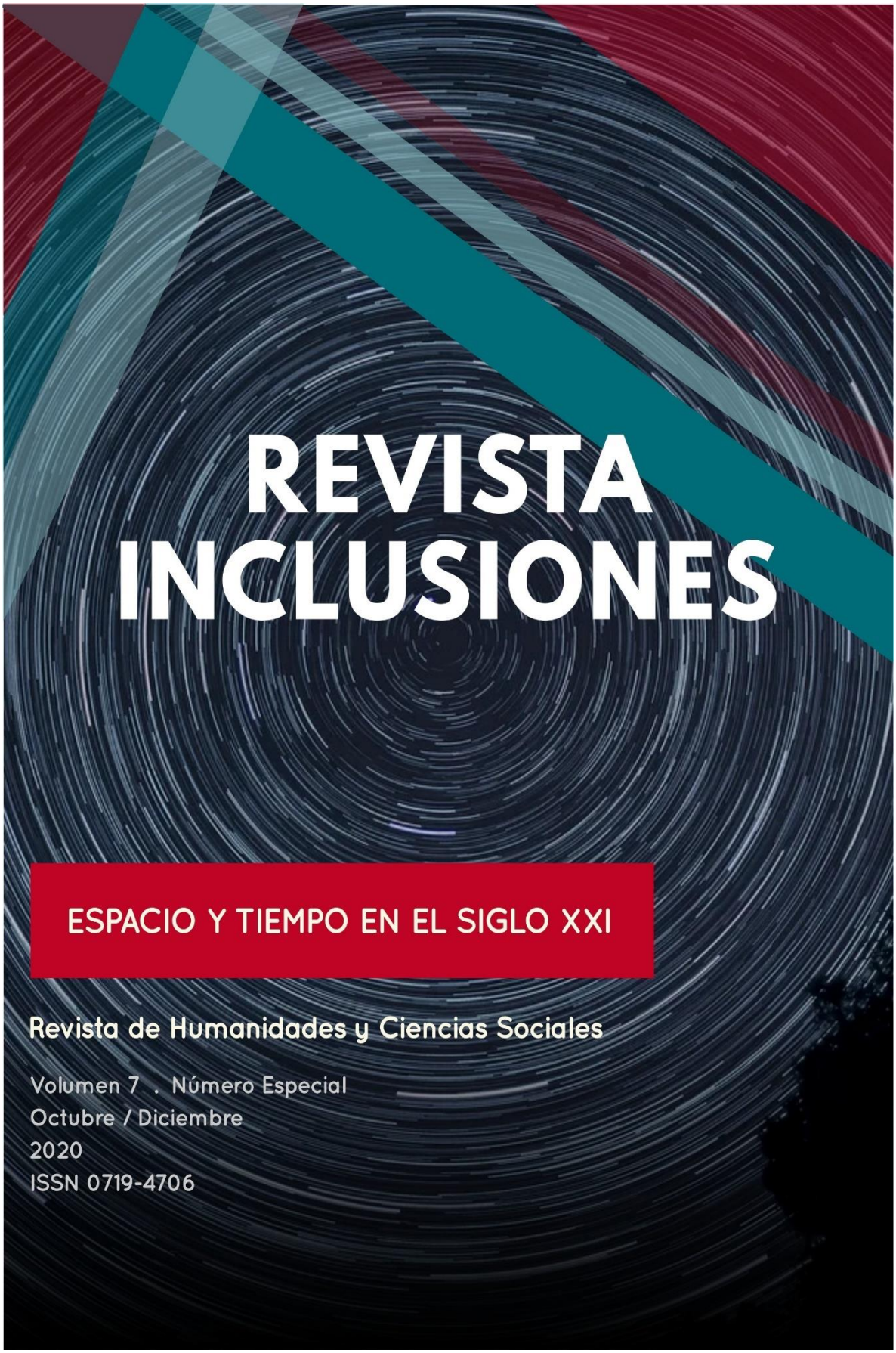
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EPIDEMIOLOGY OF BRUCELLOSIS OUTBREAKS – LITERATURE REVIEW

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Abstract

The relevance of the present study lies in the extremely high prevalence of brucellosis, a disease of social and economic importance. The study presents the literature review on the prevalence of human brucellosis in the world. The scientific search was conducted in the Elibrary, Google Scholar, Pubmed, Web of Science, Scopus, and Medline databases; a 15-year period was regarded (2005 to 2019). 46 articles corresponded to the objectives of the study. The present work describes the incidence and prevalence of human brucellosis in different countries and continents, the epidemiological criteria for brucellosis, and its frequency and characteristics among children. Results of surveys of risk groups to assess the level of brucellosis awareness and of risky practices are given; outbreaks and cases among travelers are described; and special attention is paid to specific factors and conditions of human infection in different regions. The following conclusion is made: successful eradication of brucellosis is possible only with comprehensive programs of public health services and veterinary control combined with appropriate training programs for agricultural workers.

Keywords

Human brucellosis – Morbidity – Epidemiology – Prevention – Prevalence – Infection control

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Introduction

Human brucellosis is the most common zoonosis throughout the world, especially in the Mediterranean countries, in North and East Africa, the Middle East, South and Central Asia and Central and South America. In the countries of the Eastern Mediterranean, more than 100 cases per 100,000 people are recorded annually, with the highest rates in Syria, Lebanon, Iraq, Saudi Arabia, Sudan and Oman[1].

More than 500,000 cases of brucellosis are reported annually to the World Health Organization (WHO) from 100 countries. Brucellosis is a topical public health problem in Egypt, where seroprevalence in the Asyut Governorate is estimated at 1.29% among the general population[2].

History records an epidemic of human brucellosis in China in the mid-1950s and the 1970s; a significant decrease in the incidence was observed in the mid-1990s. However, the epidemiological situation with brucellosis worsened over the past 10 years – the number of cases increased from 6448 in 2003 to 38 151 in 2011, possibly due to frequent market fluctuations and the lack of quarantine measures[3].

Brucellosis remains one of the most common infections in the group of especially dangerous zoonoses which have a significant share in human infectious pathology. Brucellosis (synonyms: Maltese, Mediterranean, Gibraltar, Cypriot fever, undulating, typhomalarial, Bang's disease) is an infectious zoonosis caused by the bacteria under the common name Brucella. It has a high potential for becoming chronic and is characterized by systemic lesions of organs and systems; predominantly, the musculoskeletal system, nervous and reproductive systems are affected.

Brucellosis was first described in 1860 as 'Mediterranean gastric remitting fever' by British Surgeon General Jeffery Allen Marston during his stay on the island of Malta. In 1887, Scottish pathologist and microbiologist Major-General David Bruce isolated the causative agent of the disease from the spleens of five British soldiers who died in Malta, and named the bacteria *Micrococcus melitensis*. According to the international classification, the genus *Brucella* consists of seven independent species, four of which are pathogenic for humans: *B. melitensis*, *B. abortus*, *B. suis*, *B. canis*. The natural reservoir for Brucella in nature are animals; the main threat for humans are sheep, goats, cattle and pigs as carriers of the three main types of pathogen (*B. melitensis, B. abortus and B. suis*). Transmission of the causative agent and infection of people occurs through contact, nutritional and, less frequently, airborne ways; combined transmission is possible. The factors of transmission to a person from a sick animal are raw materials of animal origin (wool, down, skins), meat and dairy products, infected animal care products, excreta and other objects infected with Brucella. Humans have no epidemiological significance in brucellosis transmission.

[1] H.G. Garcell; E. G. Garcia et al., Outbreaks of brucellosis related to the consumption of unpasteurized camel milk (Published by Elsevier Limited, 2015).
[2] A. Hasanaina; R. Mahdyb; A. Mohamed & M. Ali, "A randomized, comparative study of dual therapy (doxycycline–rifampin) versus triple therapy (doxycycline–rifampin–levofloxacin) for treating acute/subacute brucellosis", The Brazilian Journal of Infectious Diseases, (2016).
[3] Liu Quan; Cao Lili & Zhu Xing-Quan, « Major emerging and re-emerging zoonoses in China: a matter of global health and socioeconomic development for 1.3 billion", International Journal of Infectious Diseases, (2014).

The present research aims to conduct a review of foreign and domestic literature on the prevalence of brucellosis among people.

Methods

This is a descriptive retrospective epidemiological study. The search regarded a 15-year period (2005-2019). The review included Elibrary, Google Scholar, Pubmed, Web of Science, Scopus and Medline publications in the state, Russian and English languages. The following keywords were used: human brucellosis, morbidity, epidemiology, prevention, prevalence.

Repeated publications, articles discussing the clinical pictire, treatment and complications of human brucellosis, as well as articles on animal brucellosis and the veterinary service were excluded from the study. 46 articles corresponded to the objectives of the study.

Results

A review of the incidence of human brucellosis in 31 provinces of China showed an annual upward trend from 2005 to 2009, and a slight decrease in 2010. In 2005, 18,416 cases were registered, followed by a sharp increase during 2008–2009. The peak incidence was in 2009 (35,816 cases reported), which is almost twice the number of cases since 2005. In 2010, a slight decrease was observed (33,772 cases), but the number of cases remained higher than in 2005-2007. At the same time, the annual incidence rate varied from 1.41 to 2.7 per 100,000 people - in 2005, it was 1.41 cases, in subsequent years there was an upward trend. In 2009 and 2010, the figure rose to 2.7 and 2.56, respectively; compared with 2005, it has tripled in 2009 and 2010[4].

Another study presents data on the incidence of human brucellosis in China from 1978 to 2015. A systematic analysis of time series of two segments (1978-2000 and 2001-2015) was made to identify the internal temporal trends of each segment. The results revealed that the annual incidence of brucellosis in humans remained relatively stable in 1978-2000 (average annual: 0.10 per 100,000), then it began to grow in 2001 (0.23 per 100,000) and increased to 4.18 per 100,000 in 2015. The incidence rate linearly increased with time compared with 2001, with an average annual incline of 0.29 times a year ($t = 20.90$, $P < 0.001$)[5].

Brucellosis is a fairly rare disease for the United States, with approximately 100–200 cases per year, usually for travelers returning from the unfavorable regions of this infection. Surveillance data show that brucellosis is detected 8 times higher in areas within 100 km of the border with Mexico than in those countries that do not border Mexico. Of the 121 cases of brucellosis in 2006, 43% occurred in Texas and California, and 6.7% in Illinois. Studies conducted in Texas and California showed that 79-95% of patients are Hispanic[6].

[4] Zhong Zhijun; Yu Shuang et al., “Human brucellosis in the People's Republic of China during 2005–2010”, International Journal of Infectious Diseases, (2012).

[5] Zhou Ting; Zhang Tao et al., “Temporal Study of Human Brucellosis in China from 1978 to 2015”. American Journal of Infection Control, (2017).

[6] L. K. Logan; N. M. Jacobs, et al., “A multicenter retrospective study of childhood brucellosis in Chicago, Illinois from 1986 to 2008”, International Journal of Infectious Diseases, (2011).

In 2010, there were only 115 cases of the disease in the United States, and most of them occurred in California or Texas (40.9%). The study by Riya Joseph, Matthew P. Crotty, Jonathan Cho, Marie H. Wilson, Jennifer Tran, Joslyn Pribble, and Leigh Hunter described the outbreak of brucellosis in Dallas, Texas – in just 6 months, 8 cases were detected. These patients were part of a larger outbreak (3 clusters, 29 patients) at the Dallas-Fort-Worth metroplex for more than 6 months. Patients were aged ≥18, all cases except 1 were confirmed by identifying *Brucella melitensis* from blood cultures using a rapid test of urea and polymerase chain reaction. The cause of the disease in all the cases was contaminated goat milk cheese imported from Mexico and consumed in the United States. Seven of 8 patients (87.5%) also stayed in Mexico for a year before the onset of the disease[7].

Numerous studies conducted in Iran proved the high prevalence of brucellosis in this country. A study from 2009 to 2015 used the Disability-Adjusted Life Years Index (DALYs) to estimate the burden of human brucellosis. To calculate DALYs, the years lived with disability (YLDs) were added to the years of life lost due to premature death (YLLs); they were calculated based on the global burden of disease (GBD) formula recommended by WHO. The results showed a tendency to an increase in human brucellosis (34.6 per 100,000 people in 2009 and 71.4 in 2015; overall incidence being 88450 in 2009 and 198030 in 2015) and in mortality (244 in 2009 and 578 in 2015). About 51% of DALYs were attributed to YLLs. The rates of morbidity and mortality associated with brucellosis are unevenly distributed among all the provinces of Iran, higher in men than in women, as noted in other works[8]. A systematic review of 56 studies to identify the prevalence of brucellosis in various provinces of Iran in 2013-2015 showed geographic differences in the prevalence of osteoarticular brucellosis with estimates ranging from 27% in regions with low risk to 36% in regions with high risk of disease[9].

In this descriptive study, data were collected from patients with suspected brucellosis who were sent to the Pathobiology laboratory Noor, Tehran from 18 of the 31 provinces of Iran during 2013-2015. Overall, brucellosis was found in 2635 of 17,103 patients (15.4%). The disease was most common in the province of Hamadan (25% of cases), in patients aged 20-39 years (41%) 67% of which were men. Brucellosis was more frequently detected in the spring season (April-May)[10].

A meta-analysis of 47 studies, conducted from 1998 to 2015 in Iran, presented the epidemiological features of brucellosis in 31,572 patients. It showed that men suffer from brucellosis more often (average 57.6% of 55.02-60.1%) than women; people in rural areas

[7] R. Joseph; M. P. Crotty et. Al., "A single-institution experience with a brucellosis outbreak in the United States". American Journal of Infection Control, (2018).

[8] M. Moosazadeh; R. Nikaeen et al., "Epidemiological and Clinical Features of People with Malta Fever in Iran: A Systematic Review and Meta-Analysis", Osong Public Health and Research Perspectives, (2016); B. Piroozi; G. Moradi, et al., «Incidence, Mortality, and Burden of Human Brucellosis and Its Geographical Distribution in Iran during 2009-2015". Iranian journal of Public health, Vol: 48 (2019): 20-27; S. A. Adetunji; G. Ramirez; M. J. Foster et al., «A systematic review and meta-analysis of the prevalence of osteoarticular brucellosis", P LOS Neglected Tropical Diseases, num 13 (1): (2019) y S. Chalabiani; Nazari M. Khodadad; R. D. Nada et al., "The Prevalence of Brucellosis in Different Provinces of Iran during 2013-2015", Iranian journal of Public health, num 48 (1) (2019): 132-138.

[9] S. A. Adetunji; G. Ramirez; M. J. Foster et al., «A systematic review and meta-analysis of the prevalence of osteoarticular brucellosis", PLOS Neglected Tropical Diseases, num 13 (1): (2019).

[10] S. Chalabiani; Nazari M. Khodadad; R. D. Nada et al., "The Prevalence of Brucellosis in Different Provinces of Iran during 2013-2015", Iranian journal of Public health, num 48 (1) (2019): 132-138.

suffer more often than in urban ones (average 68.4% of 63.6-73.2%); unprotected contact with animals and use of unpasteurized dairy products led to high risk behaviors[11].

The majority of literary sources give the results of surveys of populations related to brucellosis risk contingents[12]. The works by Jahangiry, Leila; Khazaee-Pool, Maryam; Mahdavi, and Babak studied behavioral and environmental factors for brucellosis prevention and determined the causal relationships between these factors in rural areas with a high prevalence of the disease. Multi-stage random sampling was used to select villages in the Akhar district, East Azerbaijan province in Iran, of which 400 participants were recruited. The data were collected in accordance with the PRECEDE model established in March 2016. This model consists of four stages designed to assess the health and quality of life of each participant. Standardized structured questionnaires were used to study various aspects of brucellosis prevention (predisposing, enhancing, stimulating, environmental, and behavioral factors). Path analysis was used to assess the path structure of the previous model. In general, the model corresponded well to the data (2/df = 1.10; RMSEA = .016 (CI 95%: 0.00-0.07), SRMR = .02, CFI = .99). Significant positive associations were found among the predisposing, enhancing and stimulating factors on the one hand and behavioral on the other. Predisposing factors have demonstrated significant positive associations with general health, and enhancing factors and general health have shown significant positive associations with health-related quality of life (HRQOL). The present study confirms the use of the PRECEDE model for brucellosis prevention and suggests that a high level of general health combined with enhancing factors may increase HRQOL in the zone with a high brucellosis prevalence[13].

As known, the lack of knowledge about brucellosis in livestock workers can lead to very risky practices. A cross-sectional survey was conducted in the two provinces of Mongolia, where 485 shepherds were randomly selected to participate in an interview using a structured questionnaire. The results suggest that brucellosis prevention is largely related to gender, location, use of veterinary services, exposure to television programs and knowledge of brucellosis. During this study, regional differences in knowledge and behavior were noted – herders are more likely to engage in preventive practice if they have a higher

[11] M. Moosazadeh; R. Nikaeen et al., “Epidemiological and Clinical Features of People with Malta Fever in Iran: A Systematic Review and Meta-Analysis”, Osong Public Health and Research Perspectives, (2016).

[12] L. Jahangiry; M. Khazaee-Pool; M. Babak et al., “Preventive factors related to brucellosis among rural population using the PRECEDE model: an application of path analysis”, Tropical Animal Health and Production, num 51 (2) (2019): 419-428; D. Bat-Erdene; Y-Ch. Chuang & K-Y. Chuang, „Brucellosis knowledge and preventive practices among herders in Western Mongolia”, Zoonoses and Public Health, num 66 (1) (2019): 133-139; M.E. Peck; C. Jenpanich, et al. “Knowledge, Attitudes and Practices Associated with Brucellosis among Small-Scale Goat Farmers in Thailand”, Journal of Agromedicine, num 24(1) (2019): 56-63; J. García Díeza & A. C. Coelho, “An evaluation of cattle farmers knowledge of bovine brucellosis in northeastern Portugal”, Journal of Infection and Public Health, (2013); E. Lindahl; N. Sattorov; S. Boqvist & U. Magnusson, “A Study of Knowledge, Attitudes and Practices Relating to Brucellosis among Small-Scale Dairy Farmers in an Urban and Peri-Urban Area of Tajikistan”, PLOSONE, (2018) y C. Kansiime; L. M. Atuyambe, et al., «Community Perceptions on Integrating Animal Vaccination and Health Education by Veterinary and Public Health Workers in the Prevention of Brucellosis among Pastoral Communities of South Western Uganda”, PLOS ONE, (2016).

[13] L. Jahangiry; M. Khazaee-Pool; M. Babak et al., “Preventive factors related to brucellosis among rural population using the PRECEDE model: an application of path analysis”, Tropical Animal Health and Production, num 51 (2) (2019): 419-428.

level of knowledge about brucellosis. The study showed the effectiveness of sanitary education through television programs[14].

A study aimed at identifying occupational risk factors for brucellosis among goat breeders in Thailand was conducted by interviewing 51 farmers from healthy farms. The results revealed poor awareness of livestock owners of safe farming practices and significant gaps in knowledge about the transmission of the disease to animals and humans; 53% of the respondents were beginners in goat farming, 54% were aware of a possible infection, and 91.7% said their family members were not at risk concerning the disease[15].

The Background Korean cattle brucellosis observation program was improved by pre-testing animals in May 2005 (Intervention 1), and in June 2006, it was further extended to livestock farms (Intervention 2). To quantify the time dependence between cattle and human brucellosis, an analysis of time series was conducted using data from the Korean National Notification System (2004-2014). Significant time dependencies were observed after Intervention 1 (June 2005-June 2006, without lag, = 0.57, p = 0.04) and Intervention 2 (July 2006-June 2007, 1-month lag, = 0.65, p = 0.03). Besides, after Intervention 1 (= -0.17 per 10 mil people, P = 0.03) and Intervention 2 (= -0.19 per 10 mil people, P = 0.04), significant changes in human morbidity were observed. The authors concluded that to effectively reduce the incidence of brucellosis in the population, changes are needed in the nationwide comprehensive animal observation program[16].

Brucellosis is an urgent public health problem for the Arab population in Israel and requires immediate and long-term eradication and control. The incidence among the general population in Israel has increased dramatically from 1.9 per 100,000 people in 2009 to a peak of 7.3 in 2014. Every year, 95-100% of cases occur in the Arab population, leading to the incidence increase from 10 per 100,000 in 2009 to 33.5 in 2014. During this period, at least one case of brucellosis was reported in 133 different localities, of which 20 were settlements with a high incidence for one year. In 2009-2013, the number of affected settlements ranged from 35 to 44 annually, while in 2014 there were 82 settlements throughout the country[17].

As for the economic consequences of brucellosis, the researchers Oded Vered, Tzahit Simon-Tuval, Pablo Yagupsky, Miki Malul, Assi Cicurel, and Nadav Davidovitch estimated the costs of healthcare associated with human brucellosis from the insurer's point of view. A retrospective case-control study was conducted among patients of Clalit Health Services (CHS) who were diagnosed with brucellosis at the Medical Center of the University of Soroka (Southern Israel) in 2010-2012 (n = 470). During a year after the diagnosis, the average total annual cost of HIPC for brucellosis was significantly higher than in the control group ($ 1,327 vs. $ 380, respectively, P <0.001). Most of the differences are associated with a 7.9-times increase in hospitalization costs (US $ 892 vs. US $ 113, respectively, P <0.001). In addition, compared with the control group, the hospitalization rate was

[14] D. Bat-Erdene; Y-Ch. Chuang & K-Y. Chuang, „Brucellosis knowledge and preventive practices among herders in Western Mongolia", Zoonoses and Public Health, num 66 (1) (2019): 133-139.
[15] M. E. Peck; C. Jenpanich, et al., "Knowledge, Attitudes and Practices Associated with Brucellosis among Small-Scale Goat Farmers in Thailand", Journal of Agromedicine, num 24 (1) (2019): 56-63
[16] S. Ryu; R. J. S. Magalhaes & B. C. Chun, «The impact of expanded brucellosis surveillance in beef cattle on human brucellosis in Korea: an interrupted time-series analysis", BMC Infectious diseases, 19 (201) (2019).
[17] N. Ghanem-Zoubi; S. P. Eljay; E. Anis et al., «Reemergence of Human Brucellosis in Israel", Israel Medical Association Journal, num 21 (1) (2019): 10-12.

significantly higher (27.6% vs. 5.0%, P <0.001); the average stay was also higher (6.03 days vs. 4.09 days, P < 0,001). Significant differences were found in hospitalization costs ($ 892 vs. $ 141, P <0.001), ($ 118 vs. $ 46, P <0.001), drug expenses ($ 108 vs. $ 58, P <0.001), diagnostic ($ 62 vs. $ 43, P <0.001) and expenses for laboratory tests ($ 58 vs. $ 14, P <0.001)[18] .

Brucellosis was once believed unusual in children, yet now it is recognized that people of all ages are susceptible to the disease, as described in the works[19]. Mile Bosilkovski et al. presented a retrospective analysis of medical records of 317 children with brucellosis younger than 15 years who were treated at the University Hospital of Infectious Diseases in Skopje in 1989 in an endemic region of the Republic of Macedonia. There were 201 (63.4%) boys and 116 (36.6%) girls, average age 9 years (7 months to 14 years). A family history of brucellosis was noted in 197 (62.1%) patients. In 140 cases (44.2%), brucellosis was acquired as a result of direct contact with infected animals, whereas in 10 (3.1%) patients the transmission of the disease was unknown. 132 (56.2%) schoolchildren had direct contact with infected animals, whereas preschoolers had such contact only in 17 cases (17.4%) (P <0.001)[20].

Among the 1028 cases in Van (Eastern Turkey), 3.6% were aged 3–12. Tanir et al. retrospectively analyzed 90 children with brucellosis in a children's hospital in the city of Ankara. 52 patients (57.8%) were from rural areas and 38 (42.2%) from urban areas of Turkey. In 64 children (71.1%), the infection was associated with the consumption of fresh cheese, a possible source of transmission was not detected in 26 children. Parents of 41 children (45.6%) worked on farms. The family history of brucellosis was traced in 14 (15.6%) children[21].

The authors conducted a retrospective multicenter review of brucellosis models in children from 1986 to 2008 in three tertiary care centers in Chicago, Illinois, USA. The average age was 6.5 (2-14 years old); 62% were girls, 67% were Hispanic by ethnicity and 24% were Arabic. Risk factors included living in an endemic area (86%), especially Mexico, and consumption of unpasteurized dairy products (76%)[22] .

[18] O. Vered; T. Simon-Tuval et al., “The Price of a Neglected Zoonosis: Case Control Study to Estimate Healthcare Utilization Costs of Human Brucellosis”, PLOS ONE, (2013)

[19] Z. Yumuka & D. O’Callaghan, “Brucellosis in Turkey – an overview”, International Journal of Infectious Diseases, (2011); M. Bosilkovski; L. Krteva et al., “Childhood brucellosis: Review of 317 cases”, Asian Pacific Journal of Tropical Medicine, (2015); O. Vered; T. Simon-Tuval et al., “The Price of a Neglected Zoonosis: Case Control Study to Estimate Healthcare Utilization Costs of Human Brucellosis”, PLOS ONE, (2013); A. Hasanaina; R. Mahdyb; A. Mohamed & M. Ali, “A randomized, comparative study of dual therapy (doxycycline–rifampin) versus triple therapy (doxycycline–rifampin–levofloxacin) for treating acute/subacute brucellosis”, The Brazilian Journal of Infectious Diseases, (2016) y N. Ghanem-Zoubi; S.P. Eljay; E. Anis et al., «Reemergence of Human Brucellosis in Israel”, Israel Medical Association Journal, num 21 (1) (2019): 10-12.

[20] M. Bosilkovski; L. Krteva et al. “Childhood brucellosis: Review of 317 cases”, Asian Pacific Journal of Tropical Medicine, (2015)

[21] Z. Yumuka & D. O’Callaghan, “Brucellosis in Turkey – an overview”, International Journal of Infectious Diseases, (2011)

[22] A. Hasanaina; R. Mahdyb; A. Mohamed & M. Ali, “A randomized, comparative study of dual therapy (doxycycline–rifampin) versus triple therapy (doxycycline–rifampin–levofloxacin) for treating acute/subacute brucellosis”, The Brazilian Journal of Infectious Diseases, (2016).

The clinical manifestations of brucellosis vary from asymptomatic infection to chronic forms. To assess the prevalence of brucellosis, symptoms during the year were observed in 186 children (7-12 years old) with asymptomatic forms in Kahak (Iran). Average age was 10 ± 1.72 years, 51% were boys, family history was traced in 15% of children. A total of 8 children were seropositive for brucellosis, and in subsequent follow-up, 6 of them showed symptoms of the disease. This study found that as many as 4.3% of children in endemic areas may have asymptomatic brucellosis, and many of these children may develop symptoms of the disease in the short term[23].

In Tanzania, a cross-sectional study was conducted with a survey of 370 children with febrile conditions observed at Kilos District Hospital, among them 85 (23.0%) had malaria, 43 (11.6%) had preliminary acute leptospirosis; suspected acute brucellosis caused by *B . abortus* was identified in 26 (7.0%) and by *B. melitensis* in 57 (15.4%) patients[24].

Special attention in the literature is given to the description of brucellosis outbreaks. Family history of brucellosis was noted in[25].

Humberto G. Garcell et al. reported on a brucellosis outbreak that occurred after consuming camel milk in 15 family members in Israel, on a group contamination associated with consuming raw cheese in Lebanon, and there are reports of outbreaks in Saudi Arabia, Mexico, Malaysia and Greece[26].

The case histories of 97 patients diagnosed with brucellosis who received treatment at the Ankara Hematology Oncology Hospital from 2000 to 2010 were retrospectively studied. Data analysis included demographic data, symptoms, objective data, laboratory data, schemes and results of treatment. Consumption of unpasteurized milk or dairy products was significantly more common in patients with a family history of brucellosis (96.9%), while the remaining patients had raw milk intake in 72.3%, ($p = 0.004$). The disease was most frequently recorded in spring and summer (65%)[27].

Pregnant women with brucellosis can have serious complications and adverse obstetric consequences, including death of the fetus. This paper describes the obstetric outcomes during pregnancy in women with active brucellosis observed at the Heredia National Hospital from 1970 to 2012. 11 cases were detected; of these, 27.7% were threatened with abortion or preterm birth, 12.8% experienced spontaneous abortions,

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[23] M Aghaali; S, Mohebi & H. Heydari, “Prevalence of Asymptomatic Brucellosis in Children 7 to 12 Years Old”, Interdisciplinary Perspectives on Infectious Diseases, (2015).

[24] B. Chipwaza; G. G. Mhamphi et al., “Prevalence of Bacterial Febrile Illnesses in Children in Kilosa District, Tanzania”, PLOS Neglected Tropical Diseases (2016)

[25] T. Yoldas; H. Tezer; A. Ozkaya-Parlakay & T. R. Sayli, “Clinical and laboratory findings of 97 pediatric brucellosis patients in central Turkey”, Journal of Microbiology, Immunology and Infection, (2014); H. G. Garcell; E. G. Garcia et al., Outbreaks of brucellosis related to the consumption of unpasteurized camel milk (Published by Elsevier Limited, 2015); M. Bosilkovski; L. Krteva et al., “Childhood brucellosis: Review of 317 cases”, Asian Pacific Journal of Tropical Medicine, (2015) y M. Aghaali; S. Mohebi & H. Heydari, “Prevalence of Asymptomatic Brucellosis in Children 7 to 12 Years Old”, Interdisciplinary Perspectives on Infectious Diseases, (2015).

[26] H. G. Garcell; E. G. Garcia et al., Outbreaks of brucellosis related to the consumption of unpasteurized camel milk (Published by Elsevier Limited, 2015).

[27] T. Yoldas; H. Tezer; A. Ozkaya-Parlakay & T. R. Sayli, “Clinical and laboratory findings of 97 pediatric brucellosis patients in central Turkey”, Journal of Microbiology, Immunology and Infection, (2014)

premature delivery occurred in 13.9% of patients, fetal death was diagnosed in 8.1%, and newborns with congenital malformations in 1.1% of women. There was one maternal death because of severe sepsis. After birth, the death of newborns was in 8.1% of cases, low birth weight in 14.5%, and congenital brucellosis in 6.4%. The degree of complications decreased if treatment started within 2 weeks after the onset of the disease ($p < 0.001$). Therefore, all clinical cases with unexplained spontaneous abortions should be investigated for brucellosis[28].

Laboratory cases of human infection were established in Taiwan in 1978 in a graduate student who worked with infected material. The only outbreak occurred in 1979, when 16 people including nine laboratory workers, six dairy farm workers and one veterinarian were infected[29].

Transmission of brucellosis through body fluids during labor was documented earlier. Tijera Bell, Whitney Thorpe and Prinu Gabriel described the first case of brucellosis in a pregnant patient in Texas. The Center for Disease Control made recommendations to medical personnel on the choice and use of personal protective equipment, and requirements for the collection, storage and transportation of samples. 50 employees of the hospital were observed for six months; no diseases among them were detected. Conclusions: the risk of infection of personnel with brucellosis through body fluids during labor is minimal[30].

Several scientific papers described asymptomatic brucellosis infections in high-risk people. Thus, the examined people from Jilin Province (endemic for human brucellosis in China) did not have typical clinical signs of brucellosis but were in prolonged contact with animals and/or their products. The results showed that about 45% (135 of 300) patients had positive titers for antibodies to Brucella. Brucella DNA was detected in 25% (25 of 100) blood samples. This data implies that asymptomatic infection exists in people at high risk and that some patients with prolonged contact with animals have a chronic infection. The presence of Brucella DNA in the blood samples of these patients suggests that they are in the stage of active infection or recovery[31].

The so-called traveler brucellosis and imported cases from other border states are described in[32]. In developed countries, brucellosis began to register due to increased international travel or the importation of livestock products from endemic countries. Thus, in Taiwan, cattle brucellosis was eliminated in 1989, and regular serological surveys of farm animals indicated a prosperous epizootic situation. In 2011, from May to September, the first four cases of human brucellosis after 30 years were reported, cases occurred with tourists returning from endemic regions[33].

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In Togo, animal brucellosis was first recorded in the 1960s. Although studies on the seropositivity of brucellosis in cattle and the identification of Brucella sp. were conducted in the 1980s and the early 1990s, there was no simultaneous assessment of the incidence of humans and animals. The Savannah region is Togo's main livestock area; being the northernmost of the five administrative regions, it borders Ghana to the west, Burkina Faso to the north and Benin to the east. Cross-border movement of cattle is an integral component of livestock management practices which use mostly unregulated trade routes or cattle runs. In 1998, the member countries of the Economic Community of West African States (ECOWAS) agreed on a formal policy on livestock transportation in West Africa. The epidemiological situation in the Savannah region depends on the brucellosis situation in neighboring countries, since the Togo government allows the importation of animals from January to May each year[34].

Brucellosis is an endemic infection for Saudi Arabia with an incidence rate of about 18 per 100,000 people annually. The overall rate of seropositivity (15%) was found among residents of the country; seroprevalence among children aged 0-14 years was 10%. The reason for the high prevalence of brucellosis in Saudi Arabia is explained by the nomadic way of life, animal husbandry, the traditional use of raw milk, and the high percentage of animals imported from Africa which is endemic for brucellosis[35].

Although the incidence has decreased markedly in industrialized countries, brucellosis remains an important public health problem in many developing countries. Saudi Arabia is hyperendemic for brucellosis, with a frequency of 5.4 per 1000 people annually. Its prevalence varies in different regions of the country, with more than 8000 cases reported annually by health authorities [36].

Brucellosis is endemic in all the countries bordering Turkey; the recent political and social unrest in these countries once again emphasized this problem. Thus, in Iraq, the prevalence of brucellosis in humans is 278.4 cases, in Iran 238.6 cases per million. Syria has the highest recorded incidence of human brucellosis in the world, with 1603.4 cases per million. However, until the 1980s, cases of human brucellosis were rarely reported in Turkey. Thus, between 1930 and 1980, less than 2,000 cases were confirmed. Between 1980 and 2005, 189,226 cases of human brucellosis were reported; about 90,000 of them were registered between 2000 and 2005 (approximately 15,000 cases per year). However, these data do not reflect the actual figures, since the estimated ratio of registered and unregistered cases is about 1: 30,54. Other studies reported the results of a serological study of the population of Turkish cities in 1991 and 2005: Afyon (15.7%), Malatya (2.9%), Denizli (6.5%), Kayseri (3.4%), Bolu (1.3%) and Van (26.7%) [37].

In the Republic of Macedonia (in addition to the strategy based on the policy of testing and slaughter of seropositive small ruminants), after assessing the situation, these animals were vaccinated against brucellosis with *B. melitensis* Rev 1 vaccine in 2008.

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A retrospective study to compare the incidence of human brucellosis in three regions was performed depending on the vaccination procedure in sheep and goats one year prior to vaccination (2007) and 4 years later. It revealed that the greatest decrease in the incidence of human brucellosis (from 124.3 to 19.7 per 100,000 inhabitants) was registered in Region 3 where mass vaccination of sheep and goats was carried out. Periodic prevalence of brucellosis in sheep and goats before vaccination was 6882 per 100,000 specimen, and 3,698 after vaccination ($p < 0.05$). There is a moderate positive correlation between the number of infected people and infected sheep and goats ($r = 0.26$). Thus, vaccination was a sufficient preventive measure to control brucellosis in three regions[38].

The majority of the literary sources present the results of surveys of risk groups. 154 farmers from the municipality of Vila Real (Northern Portugal) were interviewed to assess the level of sanitary knowledge. Respondents working with infected animals (odds ratio (OR) 5.5, confidence interval 95% 1.6, 19.5) more often had a deeper knowledge of brucellosis in cattle. 25.3% of respondents did not know that brucellosis is transmitted from cattle. Half (54.5%) of respondents believe that brucellosis in cattle is a treatable infectious disease, which was due to the lack of veterinary care on the farm (60.4%). Successful eradication of brucellosis is possible only if there are adequate training programs for farmers (including biological protection of farms), legal programs and veterinary public health programs[39].

Researchers conducted a cross-sectional study for six weeks in 2011, using descriptive statistics and a logistic regression model to assess knowledge of brucellosis of 441 farmers living in urban and suburban areas of Dushanbe in Tajikistan. Most farmers (85%) never heard of brucellosis; this low awareness was associated with their low level of education ($P = <0.001$). Respondents who had no animal health problems knew little about brucellosis compared with those who often applied to the veterinary service ($P = 0.03$). It was also noted that about 30% of households regularly consume and 17% of households sell unpasteurized dairy products, and the majority of respondents do not use means of protection when handling abortion animals and their materials. The poor knowledge of farmers about brucellosis and risky behavior dictates the need to include health education in disease management programs[40].

Researchers from Uganda conducted six focus group discussions (FGD), two from each sub-district, one with local leaders and the other with pastoralists and farmers, and five key informational interviews with two public health workers and three veterinary workers from three sub-districts in Kiruhura district. All the results were analyzed using the data analysis method of hidden content, and it revealed that respondents had limited knowledge of brucellosis. Combating human brucellosis involves integrating the efforts of the Government and all the other interested parties such as workers from the veterinary, medical and public health sector[41].

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The countries of Central Asia that are part of the CIS have one of the highest global incidence rates of brucellosis in people: Kazakhstan – 11.6, Kyrgyzstan – 36.2, Tajikistan – 11.6, Azerbaijan – 5.3 per 100,000 people[42].

Brucellosis is a social problem in the group of focal zoonotic infections in the Russian Federation. Deer brucellosis poses a risk to people working in the industry, as well as consuming venison. The infection rate among deer varies from 0.9-60.0% in Taimyr to 1.2-12.4% in the Evenk Autonomous District, to 1.0-35.7% in Chukotka and up to 60% in Yakutia. Of the 14 administrative districts of the Magadan Oblast, 11 were recognized to be high risk of reindeer brucellosis. It was described that up to 10.5-23.0% of the indigenous population of Yakutia and the Far East working at reindeer herding plants in the past were infected with brucellosis pathogens. Since 1997, the incidence of brucellosis decreased significantly, with now only rare cases recorded in these areas[43] .

A large retrospective study was conducted in the Stavropol Krai for 2000-2014. In the North Caucasus Federal District, the largest number of new brucellosis cases was registered in the Republic of Dagestan (59.3%) and the Stavropol Krai (27.4%). The incidence of brucellosis in the Stavropol Krai was 5-10 times higher than in the Russian Federation as a whole. The true prevalence of brucellosis was 25% more than statistical data in terms of its clinical forms which were not included in the official registration. There is a reduction tendency in occupational brucellosis. At the same time, brucellosis accounts for 75% of the total number of occupational diseases in the territory[44].

Outbreaks of brucellosis in this region are also described: in 2010-2016, 578 cases of newly diagnosed brucellosis in people with an incidence rate of 2.88 per 100,000 were recorded. In 2016 in Essentuki, a focus was identified with 15 cases[45]. In the outbreak in the Voronezh Oblast in 2009 (10 people), there was a high proportion of occupational pathology (73.7%), the highest incidence was recorded among fattening and machine milking operators (26.3 and 15.8%, respectively), and also in veterinarians (31.6%)[46].

Works by A.M. Skogoreva et al. and by Yu.G Pritulina et al.[47] analyzed the epizootic and epidemic situation for brucellosis in the Russian Federation, Central Federal District and Voronezh Oblast in 2008-2017 and established a slow steady increase in the number of outbreaks at different levels. According to the Central Federal District, the highest number of people with brucellosis in 2008-2017 was in Moscow (79 cases) and the Voronezh Oblast

[42] D. G. Ponomarenko; D. V. Rusanova et al., « Overview of the epizootic and epidemiological situation of brucellosis in the Russian Federation in 2017 and the forecast for 2018", Problems of especially dangerous infections, num 2 (2018): 23-29.

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(35 cases). The proportion of professional human brucellosis in the Voronezh Oblast is 1.9 times higher than the average for the Russian Federation; the incidence of veterinary specialists is also 3.6 times higher than the average in the country, while the percentage of household plots and workers who are not directly associated with animals is 1.9 times lower.

The epidemiological manifestations of brucellosis in various regions of the Russian Federation for 1997-2007 were studied. Brucellosis of animals and people was registered in 59 (67%) subjects of the Russian Federation. The largest number of patients is concentrated in the Southern (68%) and Siberian (20.9%) federal districts. 75% of cases in the country were in farms with a joint housing of various animal species in the North Caucasus and Eastern Siberia where *B. melitensis* migrated to cattle. The epidemic manifestations of modern brucellosis are associated with socio-ecological factors and include the predominance of acute forms of the disease with isolation of cultures of *B. melitensis*, pronounced seasonality, involvement in the epidemic process and lack of connection with professional activities in animal husbandry[48].

Certain studies reveal the relationship of incidence with vaccination of animals. Thus, in 2003-2009 in the Russian Federation, specific immunoprophylaxis of animal brucellosis was carried out on the territory of 36 subjects, mainly in the public sector farms where sheep brucellosis was recorded. The population contingent at risk was vaccinated in the territory of 25 subjects, in 16 of them together with the immunization of animals. Immunoprophylaxis in small ruminants and cattle in the public livestock sector led only to an insignificant decrease in new cases of human brucellosis (1.2 times); vaccination of animals, including in private households, and risk groups, reduced the incidence of people by 1.5 times. When only public households cattle and the population at risk were vaccinated, the incidence, on the contrary, increased 1.6 times, which was caused by brucellosis in private household sheep which did not receive specific vaccination. Conducting specific immunoprophylaxis only in risk groups did not affect the incidence of people. The lack of effectiveness of specific immunoprophylaxis is associated with the socio-economic recession in the 90s and with the lack of fundamental changes in the system of epizootological and epidemiological surveillance (taking into account the diversity of ownership forms in animal husbandry)[49].

Kazakhstan, a state located in central Eurasia, is among the states with a high brucellosis incidence – among the CIS countries, it ranks second after Kyrgyzstan. Changes in veterinary standards and control strategies with full coverage of livestock testing, followed by the slaughter of seropositive animals, did not have a significant effect on the level of infection. Since 1991, the incidence of brucellosis in sheep has steadily decreased and stabilized at around 0.1–0.3% by 2011. In contrast to the reduction in the livestock of sheep, the incidence of people steadily increased from 11.3 per 100,000 people in 1990 to 19.2 in 1992 and reached its peak (23.95 per 100,000 people) in 2004 [50].

Over the past decades, a number of brucellosis eradication programs were implemented in the country. By 2012, efforts to combat infection led to a decrease in the prevalence of seropositive animals and, as a result, the incidence of human brucellosis in

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Kazakhstan, which was 17.5 per 100,000 people in 2006 and decreased to 8.49 in 2013. The distribution of the brucellosis incidence is uneven throughout the territory, and the authors identified zones with minimal, medium and high incidence using GIS technology[51]. However, as known, official statistical reports do not fully reflect the true prevalence of brucellosis. The dynamics of brucellosis incidence the Republic of Kazakhstan over the 10-year period showed a more than two-fold decline – 13.2 per 100,000 people in 2010 and 6.2. in 2017. The most unfavorable epidemiological situation is observed in Zhambyl (19.1), Kyzylorda (12.2) and West Kazakhstan (12.1) regions[52]. The authors also note a negative trend – cases of human brucellosis are recorded in populations that were previously successful in terms of the incidence of farm animals, which indicates undetected facts of infection of farm animals.

Conclusions

Human brucellosis is an actual infectious disease for many world regions, especially in the Mediterranean countries, Northern and Eastern Africa, the Middle East, South and Central Asia, and Central and South America. The majority of the authors indicate that official statistical reporting does not fully reflect the true prevalence of brucellosis. The works show a clear correlation between the prevalence of the disease among the population and the incidence of brucellosis in cattle and small ruminants. Numerous scientific publications are devoted to surveys of the population, which show low awareness of farmers of brucellosis and their risky behavior in relation to infection, which is a serious obstacle to the eradication of brucellosis in many countries. Available strategies to combat brucellosis are very strict management programs, slaughtering all seropositive animals, vaccinating healthy animals and spreading knowledge about brucellosis. The materials of the present study are of practical value for researchers in the epidemiology of infectious diseases, epidemiologists and public health specialists for identifying ways of infection, risk factors, risk groups and developing strategies to control and eradicate the disease in specific conditions.

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