JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

The Armenian SORT IT Course

Acute and chronic brucellosis eleven-year audit from a tertiary hospital in Armenia

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Abstract

Introduction: The incidence of brucellosis in Armenia in 2010 was twice as high as in other countries of the Caucasian region and has almost doubled over the last three decades. This study aimed to investigate factors associated with acute or chronic forms of presentation of human brucellosis.

Methodology: Retrospective study using data from medical records of 455 patients hospitalized for the first time at the Nork Republican Infectious Disease Referral Hospital in Yerevan, Armenia between the years 2006 and 2016. We undertook descriptive analysis of cases, compared acute and chronic cases, and identified factors associated with acute and chronic cases using regression.

Results: The majority of brucellosis cases had acute case presentation (73.0%), were males (70.3%), between the ages of 20-60 years (66.2%) and unemployed (89.9%). About two-thirds of cases reported a history of consumption of raw unpasteurized milk. The multivariate analysis revealed that factors associated with the form of brucellosis were age, symptom duration preadmission, fever, antibody titer, and hospitalization outcomes.

Conclusion: This study revealed that brucellosis is unevenly distributed across different age groups, as well as regions of Armenia. Affected individuals did not seek medical attention after the onset of the symptoms for about 2 months. Therefore, the targeted educational campaigns could be of crucial importance to prevent the disease in humans, contribute to its early diagnosis and treatment.

Key words: Brucellosis; SORT-IT; operational research; Armenia; zoonosis.

J Infect Dev Ctries 2019; 13(5S):042S-050S. doi:10.3855/jidc.10934

(Received 08 October 2018 – Accepted 26 February 2019)

Introduction

Brucellosis is the collective name given to a group of zoonosis causing prolonged convalescence which can result in adverse economic and health outcomes for patients [1]. The three clinical forms of human brucellosis, acute, sub-acute and chronic, manifest over different periods. Acute brucellosis (symptoms persisting up to three months) develops in approximately half of cases, while chronic cases (symptoms for more than six months) require prolonged chemotherapy treatment and can result in additional burdens on the patient and the health care system [2]. In the majority of cases, brucellosis presents with non-specific symptoms such as fever, sweating, anorexia, appetite loss and profound muscle weakness. It can also involve specific tissue and organs causing osteo-articular, urogenital, neurological and cardiological complications [2,3].

Globally, up to 500,000 new cases of brucellosis are reported annually [4]. Brucellosis is endemic throughout the Mediterranean region and the Middle East, with incidence estimates more than 100 cases per 100,000 person-years in Iraq, Jordan, and Saudi Arabia [5]. The incidence of brucellosis in central Asian countries is similarly high [6].

In 2010, the incidence of brucellosis in Armenia was two times higher (9.54 cases per 100,000 population) than in two neighboring countries (Azerbaijan 3.98 and Georgia 4.55 per 100,000 population). In Armenia, the incidence rate has increased almost doubled over the past three decades: 5.1 and 9.2 per 100,000 population in 1990 and 2016, respectively [7]. In 2012, the Armenian Center of

Disease Control reported 112 outbreaks of cattle and 61 outbreaks of caprine brucellosis, with 93.2% of human brucellosis cases occurred in rural communities [8]. There is conflicting evidence on whether prevalence in Armenia is higher in men [9] or women [10]. In 2016, the evaluation of the burden of brucellosis conducted in Nork Republican Infectious Disease Referral Hospital, Yerevan, Armenia (NRIDRH) revealed that the economic losses for the hospital were around 36 million Armenian Drams (currency in Armenia) per year (approximately 74,000 USD) [11].

Based on a literature review and consultation with the Armenian Center of Disease Control and Ministry of Agriculture, we identified remaining gaps in the evidence on brucellosis epidemiology and disease control response. This includes data related to the routes of transmission, species type, regional distribution of cases, timeliness of cases accessing specialized infectious disease care, and treatment outcomes. Such evidence is essential to inform improvements in case detection and early treatment of human brucellosis in the Republic of Armenia. Without policy improvements, brucellosis may continue to be a public health concern.

Therefore, we aimed to investigate factors associated with acute or chronic forms of human brucellosis at the NRIDRH in Yerevan, Armenia, during the period from 2006 to 2016, among the cases hospitalized for the first time.

The specific objectives of this study were: (1) to describe the demographic, epidemiological, and clinical characteristics of brucellosis cases hospitalized to NRIDRH for the first time during the period from 2006 to 2016; and (2) to compare demographic, epidemiological, and clinical factors and hospitalization outcomes by the form of brucellosis (acute, chronic), as well as identify the factors associated with it.

Methodology

Study design

We utilized a retrospective study design to investigate the medical records of patients diagnosed with brucellosis for the first time between 2006 and 2016 at the NRIDRH in Armenia. We included medical records for brucellosis cases diagnosed for the first time between 2006 and 2016, with no exclusion criteria.

Study Setting

Armenia's population of approximately 3 million resides in both urban and rural areas across 11 marzes (provinces) with diverse geographical features (plains, valleys, hills and high mountains) [12]. According to the Ministry of Agriculture of Armenia, cattle breeding is the leading sector of the Armenian livestock industry; 95% of the milk produced in the country and about 55% of the meat is obtained from cattle breeding [13].

Study site

The NRIDRH, an infectious disease hospital, is one of the largest medical centers in the Republic of Armenia located in the capital city, Yerevan. The hospital provides inpatient and outpatient services for both adult and pediatric patients, treating up to 8,000 patients per annum.

Study instruments and data collection

From November 2017 to March 2018, clinicians trained in public health and research ethics identified all medical records from the study period diagnosed with brucellosis. Data were extracted using the US Center for Disease Control's case report form for brucellosis [14].

Data management and analysis

Statistical analysis was conducted using web-based statistical application Easystat.app available at https://easystat.app/. In defining our variables, we defined absence of an epidemiological factor in the clinical notes as absence of the factor in the case history, rather than a missing value. We defined three *age* categories (less than 20, 20 to 60, and above 60 years) based on cut points that were found using LOWESS smoothing analysis aimed to identify the cut points where the relationship between the response variable and predictor is expected to be changed [15]. We defined *employment status* as a binary variable of current employment status upon admission. For exposure to potential animal carriers of brucellosis, we defined type of exposure in relation to cattle, goat, sheep or any other, which included swine, donkeys, horses, pigeons, ducks, other birds, cats, dogs, bats, and rodents. We defined *any joint pain* as presence of joint pain and large joint pain, which included knee, sacroiliac, shoulder and ankle joints. Symptom onset in days was defined based on patient report of symptom duration preadmission, and outliers ($\geq$ 730 days, n = 23 cases) were excluded from analysis. Hospitalization outcome was defined as binary variable of illness progress (improved/unchanged) by the clinician at the moment of discharge from the hospital. We defined cut points for length of hospital stay using LOWESS smoothing test, which resulted in three subcategories (less than 10, 10 to 20, and above 20 days).

Table 1. Demographic, epidemiological, and clinical characteristics of brucellosis cases in first admission to Nork Republican Infectious Disease Hospital, 2006-2016.

Characteristics	Brucellosis cases, N = 455	
	n	%
Demographic characteristics		
Age, years (mean ± SD)	32.5 ± 17.8	
Age groups, years:		
< 20	123	27.0
20-60	301	66.2
> 60	30	6.6
Male Gender	320	70.3
Rural residence	259	56.9
Region of origin:[a]		
Yerevan	146	32.0
Kotayk	77	17.0
Aragatsotn	62	13.6
Employed at time of admission	46	10.1
Epidemiological characteristics		
Exposure to animal carriers:		
Any animal carrier:	76	16.7
Cattle	53	69.7
Goat	32	42.1
Sheep	54	71.1
Any other animal carrier	9	11.8
Contact with animal abortus material	75	16.4
Consumption of raw milk	288	63.3
Consumption of undercooked meat	87	19.1
Contact with a person with brucellosis symptoms	57	12.5
Symptoms present upon admission		
Fever	215	47.3
Sweating	318	69.9
Urogenital tract infection	39	8.6
Muscle soreness	67	14.7
Appetite loss	117	25.7
Rigor	56	12.3
Presence of joint pain	366	80.4
Large joint pain	249	54.7
Knee	139	30.6
Sacroiliac	91	20.0
Ankle	52	11.4
Shoulder	49	10.8
Clinical characteristics and outcomes		
Brucellosis diagnosis type:[b]		
Acute	332	73.0
Chronic	123	27.0
Brucellosis antibody titer:[c]		
1:50-1:100	28	6.2
1:200-1:400	270	59.3
1:800-1:3200	124	27.3
Length of hospital stay, days (mean ± SD)	9.3 ± 5.1	
Duration of symptoms prior to admission, days (mean ± SD)[d]	62.1 ± 93.0	
Hospitalization outcome:		
Improvement	437	96.0
Unchanged	13	2.9

SD: standard deviation; [a] Only three provinces with the highest frequency of brucellosis cases presented; [b] Sub-acute brucellosis cases were excluded from the analysis based on the small frequency (n = 3); [c] Dilution of patient serum; [d] The outliers (n = 23) ≥ 730 days were excluded from the analysis.

We distributed antibody titer results, detected by serial dilutions method, across three groups (1:50 to 1:100, 1:200 to 1:400, and 1:800 to 1:3200) [16]. We described demographic, epidemiological, clinical characteristics; symptom duration preadmission; length of stay, diagnostic procedures, and hospitalization outcomes for brucellosis cases for categorical variables using number of cases and their frequencies and continuous variables using means and standard deviations. We compared demographic, epidemiological, and clinical factors and hospitalization outcomes between acute and chronic brucellosis groups in proportions of independent variables using Pearson's chi-square test or non-parametric Fisher's exact test, as necessary. We assessed the strength of association between each independent continuous variable and the outcome variable using Student's *t*-test. The missing values were excluded from analyses and the level of significance was set at 5% (p-value ≤ 0.05). We used multiple logistic regression analysis to measure the strength of associations between the independent variables, and the dependent variables as well as test for effect modification while controlling for potential confounders.

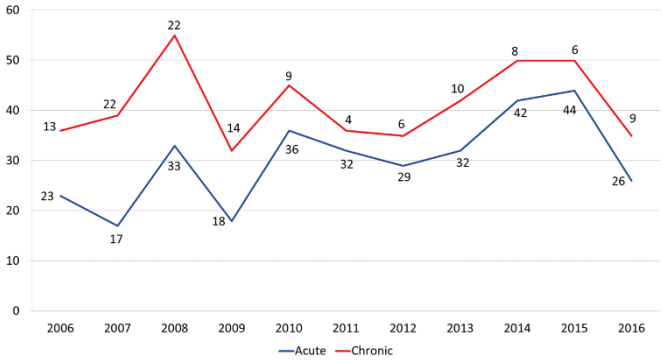
Ethics Approval

The Institutional Review Board of Center of Medical Genetics and Primary Health Care provided scientific and ethical approval for the study protocol.

Results

A total number of 458 eligible cases were identified, including three with sub-acute brucellosis, which we excluded based on the small frequency of cases (less than 5), resulting in a total number of 455 brucellosis cases in the final analysis. The mean age (± standard deviation, SD) was 32.5 ± 17.8 years with two-thirds between 20 and 60 years. The majority of cases were males (n = 320, 70.3%) and from rural areas (n = 259, 56.9%). Most cases originated from Yerevan (n = 145, 32.0%), followed by marzes of Kotayk (n = 77, 17.0%) and Aragatsotn (n = 62, 13.6%) with the majority of cases being not employed at the moment of admission (n = 409, 89.9%). Almost one fifth (16.7%) of cases reported exposure to any animal carrier, among which sheep (71.1%), cattle (69.7%) and goat (42.1%) were the most frequent. A large proportion of cases had a history of consumption of raw unpasteurized milk (n = 288, 63.3%), while consumption of undercooked meat, contact with a person with similar symptoms, involvement in the slaughter of animal were indicated for less than 20% of cases.

Figure 1. Distribution of acute and chronic brucellosis cases in first admission to Nork Republican Infectious Disease Hospital, 2006-2016.



Most common symptoms reported upon admission were joint pain (80.4%), the majority of which included large joints (54.7%)), sweating (69.9%), and fever (47.3%), while the least common was urinary tract infection (8.6%). The majority of cases (n = 332, 73.0%) presented with acute brucellosis. The most common (59.3%) antibody titer detected by serial dilutions was in the range of 1:200 to 1:400.

The mean (± SD) length of hospital stay was 9.3 ± 5.1 days, with a maximum length of 32 days. On average, symptom duration before admission was 62.1 ± 93 days, with a maximum duration of 639 days. In the majority of cases (96%), the hospitalization outcome was recorded as improved. Detailed information on demographic, epidemiological, clinical and other characteristics of brucellosis cases included in this study is presented in Table 1, while their over-time distribution between 2006 and 2016 is presented in Figure 1. Cases with chronic brucellosis were significantly older (37.0 ± 16.5 years) than those with acute brucellosis (30.87 ± 18.08 years). However, both groups were similar to each other in terms of gender distribution, place of residence and employment status at admission.

We found a statistically significant difference between groups in reporting contact with animal carriers such as cattle (81.5% *versus* 63.3%), goat (55.6% *versus* 34.7%) and sheep (77.8% *versus* 67.3%), with chronic cases reporting more frequently ($p < 0.05$). A significant difference in reported contact with a person with similar symptoms was found, with acute cases reporting more frequently: 14.7% *versus* 6.5% ($p < 0.05$). Acute cases of brucellosis were significantly more likely to report fever and chills upon admission; while among chronic cases, joint pain, muscle soreness and urinary tract infection were significantly more common. Longer symptom duration preadmission was significantly associated with chronic brucellosis, while

the hospitalization outcome was recorded as improved significantly more frequently among cases with acute brucellosis. See Table 2 for the results of the bivariate analysis of acute and chronic brucellosis cases.

We found that after adjusting for covariates in a multivariate analysis, factors associated with the form of brucellosis were age, symptom duration preadmission, fever, antibody titer and hospitalization outcome (see Table 3). In the adjusted model, we found the odds of chronic type of brucellosis were 2.6 times higher among cases aged 20 to 60 years compared to those less than 20 years. An increase in preadmission symptoms duration of one day increased the odds of chronic brucellosis type by 1.02 times. The odds of developing fever were 2.4 times higher among acute type of brucellosis. The association between antibody titer and form of brucellosis showed a relationship between higher load and chronic brucellosis, with 1:50 to 1:100 increasing the odds of being diagnosed with chronic brucellosis 12.1 times and 1:800 to 1:3200 decreasing the odds by 70%.

Table 2. Bivariate analysis of demographic, epidemiological, and clinical characteristics by type of brucellosis in first admission to Nork Republican Infectious Disease Hospital, 2006-2016.

Characteristics	Acute cases N = 332		Chronic cases N = 123		*p*-value
	n	%	n	%	
Demographic characteristics					
Age, years (mean ± SD)	30.8 ± 18.1		37.0 ± 17.0		< 0.001
Age, years:					
< 20	102	30.7	21	17.1	-
20-60	210	63.3	91	73.9	0.005
> 60	19	5.7	11	8.9	0.018
Male Gender	238	71.7	82	66.7	0.30
Rural residence	189	56.9	70	56.9	0.10
Employed at time of admission	35	10.5	11	8.9	0.62
Epidemiological characteristics					
Exposure to animal carriers:					
Any animal carrier:	49	14.7	27	21.9	0.07
Cattle	31	63.3	22	81.5	0.011
Goat	17	34.7	15	55.6	0.008
Sheep	33	67.3	21	77.8	0.037
Any other animal carrier	6	12.2	3	11.1	0.70
Contact with animal abortus material	47	14.2	28	22.7	0.028
Consumption of raw milk	207	63.3	81	65.8	0.50
Consumption of undercooked meat	55	16.6	32	26.0	0.023
Contact with a person with brucellosis symptoms	49	14.7	8	6.5	0.018
Symptoms present upon admission					
Fever	178	53.6	37	30.1	< 0.001
Sweating	232	69.8	86	69.9	0.10
Urogenital tract infection	23	6.9	16	13.0	0.039
Muscle soreness	42	12.6	25	20.3	0.041
Appetite loss	89	26.8	28	22.7	0.39
Rigor	47	14.2	9	7.3	0.048
Any joint pain	251	75.6	115	93.5	< 0.001
Large joint pain	165	49.7	84	68.3	< 0.001
Duration of symptoms prior to admission, days (mean ± SD)[a]	33.9 ± 39.1		157.3 ± 145.3		< 0.001
Clinical characteristics and outcomes					
Brucellosis antibody titer:[b]					
1:50-1:100	10	3.0	18	14.6	
1:200-1:400	188	56.6	80	65.0	< 0.001
1:800-1:3200	113	34.0	11	8.9	< 0.001
Length of hospital stay, days (mean ± SD)	9.4 ± 4.9		8.7 ± 5.5		0.25
Hospitalization outcome:					
Improved	326	98.2	111	90.2	< 0.001
Unchanged	3	0.9	10	8.1	-

SD: standard deviation; [a] The outliers (n = 23) ≥ 730 days were excluded from the analysis; [b] Dilution of patient serum; standard tube agglutination (STA) test.

Table 3. Multivariate analysis with crude and adjusted odds ratio of the demographic, epidemiological and clinical characteristics associated with chronic brucellosis*

Characteristics	Crude OR	95% CI	*p*-value	Adjusted OR	95% CI	*p*-value
Age, years:						
< 20	1.0	-	-	1.0	-	-
20-60	2.1	(1.8, 3.7)	0.011	2.6	(1.1, 6.4)	0.034
> 60	2.2	(0.8, 6.0)	0.121	1.8	(0.4, 8.0)	0.440
Male gender	1.0	(0.5, 1.2)	0.209	1.0	(0.5, 2.1)	0.960
Rural residence	1.1	(0.7, 1.7)	0.726	1.8	(0.9, 3.7)	0.117
Employed at time of admission	0.9	(0.5, 1.9)	0.855	2.0	(0.5, 7.6)	0.293
Exposure to any animal carrier	0.8	(0.4, 1.4)	0.393	1.5	(0.2, 9.7)	0.699
Exposure to cattle	0.6	(0.3, 1.2)	0.163	0.3	(0.0, 3.0)	0.356
Consumption of raw milk	0.8	(0.5, 1.3)	0.461	0.9	(0.4, 1.8)	0.690
Consumption of undercooked meat	0.6	(0.4, 1.1)	0.105	0.7	(0.2, 1.8)	0.419
Contact with a person with brucellosis symptoms	2.6	(1.1, 6.3)	0.028	3.2	(0.9, 11.0)	0.061
Duration of symptoms prior to admission, days (mean ± SD)	-123.4 ± 14.8	(-152.8, -94.0)	< 0.001	1.0	(1.0, 1.0)	< 0.001
Fever present upon admission	2.2	(1.4, 3.5)	< 0.001	2.4	(1.2, 4.9)	0.015
Any joint pain present upon admission	0.2	(0.1, 0.5)	< 0.001	0.3	(0.1, 1.2)	0.093
Large joint pain	0.5	(0.3, 0.8)	0.002	0.8	(0.4, 1.8)	0.655
Brucellosis antibody titer:						
1:50-1:100	4.6	(1.9, 10.6)	< 0.001	12.1	(3.6, 40.9)	< 0.001
1:200-1:400	1.0	-		1.0		
1:800-1:3200	0.3	(0.1, 0.5)	< 0.001	0.3	(0.1, 0.7)	0.012
Length of hospital stay, days:						
< 10	1.0	-	-	1.0	-	-
10-20	1.4	(0.8, 2.3)	0.260	1.8	(0.8, 3.9)	0.166
> 20	0.7	(0.1, 275)	0.773	0.3	(0.0, 3.1)	0.343
Hospitalization outcome: improved	7.1	(1.5, 44.8)	0.006	11.4	(1.8, 72.6)	0.010

OR: odds ratio; CI: confidence interval; *Analysis was based on 429 cases (23 outliers of the variable "duration of symptoms (days) prior to admission" and 4 missing values of the "disease outcome" variable were excluded) to make the results more accurate and comparable.

Discussion

This was the first study conducted in Armenia that assessed an 11-year pattern in brucellosis among the patients admitted to a tertiary infectious disease hospital. To date, limited information has been available on the geographical, epidemiological, clinical and other characteristics of brucellosis cases in Armenia, despite the importance of such evidence in informing improvements in case detection and early treatment of human brucellosis. The results showed that the primary affected population is middle aged, unemployed males from rural communities. Our findings on age, gender, and rural residence likely reflect the fact that men of working age in rural areas are more involved in the care and management of the livestock in Armenia, a pattern also described in South Caucasus region [17,18]. Population-based, cross-sectional studies conducted in Mongolia, Georgia and Egypt have defined brucellosis as endemic in rural areas [19,20] and found a higher infection rates among males [21].

Our finding of almost two-thirds of cases reporting a history of consumption of raw unpasteurized milk is consistent with findings of studies conducted in Greece and Iran reporting 77.1% and 100% frequency of raw unpasteurized milk consumption, respectively [22,23]. However, in contrast to other studies, we did not reveal any association between the consumption of raw unpasteurized milk, undercooked meat or exposure to animal carriers and disease form [24,25]. This might be explained by variations in documentation of epidemiological exposures in our data sources.

Our findings on most common symptoms were similar to several other studies which also reported sweating (62.7-80.8%), fever (63.2-78.7%) and arthralgia (53.7%-70.2%) as common symptoms in brucellosis cases [26-28]. In a retrospective evaluation of 164 brucellosis cases of brucellosis in Bursa, Turkey, Kazak et al. (2016) reported that the most cases of chronic brucellosis had focal involvement such as large joint pain and urinary tract infection, similar to the findings of the present study [29].

In our study, laboratory characteristics were derived from data produced with the standard tube agglutination (STA) test. The antibody titer measured by STA test confirmed the results of similar studies [30].

Polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA) have not been used for diagnosis of brucellosis during the included time period of our study. However, for proper and accurate diagnosis some studies emphasize the importance of using several tests [31]. For example, PCR and ELISA not only detect, but also differentiate between acute, chronic and subacute forms of infection [32-35]. Currently, no medical laboratory in Armenia has the capacity to provide isolation of Brucella in a safe condition without the risk of accidental exposure. Therefore, we cannot isolate the species type of Brucellas in laboratory condition.

The results of our study showed that cases of brucellosis experience symptoms on average for about two months before accessing the appropriate treatment. Furthermore, the longer the duration of reported symptoms before admission, the greater the likelihood that a case has been diagnosed as chronic, thus increasing the chances of developing complications and prolonging the duration of treatment durations, sometimes with unfavorable outcomes [29]. This national surveillance data analysis complemented the findings from a survey conducted in Germany to investigate the trends in human brucellosis epidemiology, which also confirmed that the longer the delay in diagnosing brucellosis, the higher the probability of developing focal complications with unfavorable treatment outcomes [36]. Hence, the timely detection, early diagnosis and care are essential in brucellosis management.

The *strengths* of this study include the utilization of a single data source over a long period of time, 11 years, as well as the inclusion of all ages of brucellosis cases. However, our study is *limited* by the use of convenience sampling for the selection of the study site, which means that our results are neither nationally representative nor generalizable. For example, geographic proximity of the study site led to a high proportion of cases in this study sample from Yerevan and neighboring regions. Furthermore, limited information is available on whether any diagnostic guidelines and/or protocols were implemented in the study site during the study period of time. Thus, non-differential misclassification is one of the expected limitations of this study (a few sub-acute cases being another indication of this event).

However, due to limited existing evidence, which might also be explained by variations in documentation of epidemiological exposures in our data source, the results of our study are still important for understanding the epidemiological characteristics and hospitalization outcomes of brucellosis in Armenia.

Conclusion

In summary, this study demonstrated that brucellosis is unevenly distributed across different age groups of the population, as well as across different regions of Armenia. Affected individuals did not seek medical attention after the onset of the symptoms for about two months. The most commonly reported mode of transmission was consumption of raw unpasteurized milk.

Brucellosis has a significant public health impact on society. Misdiagnosis of human brucellosis often results in delays in treatment, with subsequent medical complications if untreated. In addition, a misdiagnosis also leads to unreported human cases, masking the magnitude of the public health burden and the required response. Infected persons suffer from deteriorated health and socioeconomic status, compromised leisure time and productive years of life due to disease.

Hence, while the early diagnosis and treatment are essential to address the burden of the disease of human brucellosis in Armenia, its prevention by raising the awareness, especially targeting middle-aged males in rural areas, as well as improving epizootic control remain paramount. The study also identified the need for the development and implementation of national guidelines/protocol for the diagnosis and treatment of brucellosis. This recommendation is in line with the current policies and practice of the Ministry of Health.

Acknowledgements

This research was conducted through the Structured Operational Research and Training Initiative (SORT IT), a global partnership coordinated by the Special Programme for Research and Training in Tropical Diseases at the World Health Organization (TDR). This specific SORT IT uses on-line videos http://www.theunion.org/what-we-do/courses/online-and-multimedia-training/sort-it developed jointly by the International Union Against Tuberculosis and Lung Disease (The Union) and Médecins sans Frontières (MSF). The specific SORT IT program that led to these publications included a partnership of TDR with the European Tuberculosis Research Initiative (ERI-TB) at WHO Regional Office for Europe and was implemented by: Tuberculosis Research and Prevention Center Non-Governmental Organization Armenia, National Tuberculosis Control Center of the Ministry of Health of Armenia, the Republican Scientific Medical Library of Armenia, Fund for Armenian Relief USA, Center of Medical Genetics and Primary Health Care, Yerevan, Armenia, Alliance for Public Health, Ukraine, MSF, Luxembourg (LuxOR), Sustainable

Health Systems, Sierra Leone, and Narotam Sekhsaria Foundation, Mumbai, India.

Funding

This SORT IT program was funded by USAID and supported by implementing partners.

References

1. Corbel MJ, Food and Agriculture Organization of the United Nations, World Health Organization, World Organization for Animal Health ((2006Brucellosis in humans and animals. :Geneva: World Health Organization. Available http://www.who.int/iris/handle/10665/43597. Accessed: 03 March 2019.
2. Jia B, Zhang F, Lu Y, Zhang W, Li J, Zhang Y, Ding J (2017) The clinical features of 590 patients with brucellosis in Xinjiang, China with the emphasis on the treatment of complications. PLoS Negl Trop Dis 11: e0005577.
3. Hasanjani Roushan MR, Ebrahimpour S, Moulana Z (2016) Different clinical presentations of brucellosis. Jundishapur J Microbiol 9: e33765.
4. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV (2006) The new global map of human brucellosis. Lancet Infect Dis 6: 91-99.
5. Yacoub AAH, Bakr SS, Hameed AM, Al-Thamery AAA, Fartoci MJ (2006) Seroepidemiology of selected zoonotic infections in Basra region of Iraq. East Mediterr Heal J 12: 112-118.
6. Bonfoh B, Kasymbekov J, Dürr S, Toktobaev N, Doherr MG, Schueth T, Zinsstag J, Schelling E (2012) Representative seroprevalences of brucellosis in humans and livestock in Kyrgyzstan. Ecohealth 9: 132-138.
7. Andreasyan D, Bazarchyan A, Simonyan S, Muradyan G, Simonyan A, Matevosyan M, Torosyan A, Sargsyan Sh, Khachatryan S (2017) Health and Health Care Yearbook, RA 2017. National Institute of Health after academician S. Avdalbekyan, MoH, RA 2016: 72. Available: http://nih.am/assets/pdf/atvk/14c0b8ed94657718a8658fb0f8ae2ff6.pdf. Accessed: 03 March 2019.
8. Berger S (2019) Brucellosis in Armenia. In Berger S, Infectious diseases of Armenia – 2019 edition. Los Angeles: GIDEON Informatics. 35-36.
9. Paronyan L, Zardaryan E, Bakunts V, Gevorgyan Z, Asoyan V, Apresyan H, Hovhannisyan A, Palayan K, Bautista CT, Kuchuloria T, Rivard RG (2016) A retrospective chart review study to describe selected zoonotic and arboviral etiologies in hospitalized febrile patients in the Republic of Armenia. BMC Infect Dis 16: 445.
10. Torosyan, L., Avetisyan, L., Vanyan A (2014) Brucellosis epidemic situation dynamics in the Armenian population, 2011-2013. In Hensel A. (Ed.), Proceedings of Brucellosis 2014 International Research Conference. Berlin, Germany: Federal Institute for Risk Assessment. 166.
11. Asoyan V, Hovhannisyan A, Mkrtchyan A, Davidyants M, Apresyan H, Atoyan L, Niazyan L (2018) Evaluating the burden of brucellosis in hospitalized patients in Armenia, 2016. Online J Public Health Inform 10: e118.
12. Statistical Committee of the Republic of Armenia (2017) Statistical Yearbook of Armenia 2017. Available: https://www.armstat.am/file/doc/99504343.pdf. Accessed: 03 March 2019.
13. Armenia - Agricultural Sector (2019) Armenia Country Commercial Guide. Available: https://www.export.gov/article?id=Armenia-agribusiness. Accessed: 03 March 2019.
14. US Centers for Disease Control (2015) Brucellosis Case Report Form. Available: https://www.cdc.gov/brucellosis/pdf/case-report-form.pdf. Accessed: 15 May 2015.
15. Cleveland WS (1981) LOWESS: A program for smoothing scatterplots by robust locally weighted regression. Am Stat 35: 54.
16. Al Sekait MA (1999) Seroepidemiology survey of brucellosis antibodies in Saudi Arabia. Ann Saudi Med 19: 219-222.
17. Ismayilova R, Mody R, Abdullayev R, Amirova K, Jabbarova L, Ustun N, Jahanov M, Nasirova E, Powers M, Rivard R, Hepburn M, Bautista CT (2013) Screening of household family members of brucellosis cases and neighboring community members in Azerbaijan. Am J Trop Med Hyg 88: 929-931.
18. Akhvlediani T, Bautista CT, Garuchava N, Sanodze L, Kokaia N, Malania L, Chitadze N, Sidamonidze K, Rivard RG, Hepburn MJ, Nikolich MP, Imnadze P, Trapaidze N (2017) Epidemiological and clinical features of brucellosis in the country of Georgia. PLoS One 12: e0170376.
19. Sanodze L, Bautista CT, Garuchava N, Chubinidze S, Tsertsvadze E, Broladze M, Chitadze N, Sidamonidze K, Tsanava S, Akhvlediani T, Rivard RG, Mody R, Hepburn MJ, Elzer PH, Nikolich MP, Trapaidze N (2015) Expansion of brucellosis detection in the country of Georgia by screening household members of cases and neighboring community members. BMC Public Health 15: 459.
20. Tsend S, Baljinnyam Z, Suuri B, Dashbal E, Oidov B, Roth F, Zinstag J, Schelling E, Dambadarjaa D (2014) Seroprevalence survey of brucellosis among rural people in Mongolia. West Pac Surveill Response J 5: 13-20.
21. Jennings GJ, Hajjeh RA, Girgis FY, Fadeel MA, Maksoud MA, Wasfy MO, Sayed N El, Srikantiah P, Luby SP, Earhart K, Mahoney FJ (2007) Brucellosis as a cause of acute febrile illness in Egypt. Trans R Soc Trop Med Hyg 101: 707-713.
22. Lytras T, Danis K, Dounias G (2016) Incidence patterns and occupational risk factors of human brucellosis in Greece, 2004-2015. Int J Occup Environ Med 7: 221-226.
23. Bahador A (2012) Brucellosis: prevalence and retrospective evaluation of risk factors in western cities of Tehran province, Iran. J Bacteriol Res 4: 33-37.
24. Roushan MRH, Ebrahimpour S, Moulana Z (2016) Different clinical presentations of brucellosis. Jundishapur J Microbiol 9: e33765.
25. Almuneef MA, Memish ZA, Balkhy HH, Alotaibi B, Algoda S, Abbas M, Alsubaie S (2004) Importance of screening household members of acute brucellosis cases in endemic areas. Epidemiol Infect 132: 533-540.
26. Hasanjani Roushan MR, Mohrez M, Smailnejad Gangi SM, Soleimani Amiri MJ, Hajiahmadi M (2004) Epidemiological features and clinical manifestations in 469 adult patients with brucellosis in Babol, Northern Iran. Epidemiol Infect 132: 1109-1114.
27. Guler S, Kokoglu OF, Ucmak H, Gul M, Ozden S, Ozkan F (2014) Human brucellosis in Turkey: Different clinical presentations. J Infect Dev Ctries 8: 581-588. doi: 10.3855/jidc.3510.
28. Qehaja-Buçaj E, Namani S, Bajrami M, Ajazaj-Berisha L, Krasniqi V (2015) Epidemiological and clinical features of

brucellosis in hospitalized patients in Kosovo. Internet J Infect Dis 14: 16669.
29. Kazak E, Akalın H, Yılmaz E, Heper Y, Mıstık R, Sınırtaş M, Özakın C, Göral G, Helvacı S (2016) Brucellosis: a retrospective evaluation of 164 cases. Singapore Med J 57: 624-629.
30. Kassiri H, Amani H, Lotfi M (2013) Epidemiological, laboratory, diagnostic and public health aspects of human brucellosis in western Iran. Asian Pac J Trop Biomed 3: 589-594.
31. Alsayed Y, Monem F (2012) Brucellosis laboratory tests in Syria: What are their diagnostic efficacies in different clinical manifestations? J Infect Dev Ctries 6: 495-500. doi: https://doi.org/10.3855/jidc.2453
32. Mitka S, Anetakis C, Souliou E, Diza E, Kansouzidou A (2007) Evaluation of different PCR assays for early detection of acute and relapsing brucellosis in humans in comparison with conventional methods. J Clin Microbiol 45: 1211-1218.
33. Chen Z, Wang Y, Wang Z, Ke Y, Zhen Q, Yuan X, Zhang W, Lu Y, Yu Y, Song H, Huang L (2013) Improvement and advancement of early diagnosis of human brucellosis in window period. Clin Infect Dis 57: 322-323.
34. Mohamed Zahidi J, Bee Yong T, Hashim R, Mohd Noor A, Hamzah SH, Ahmad N (2015) Identification of Brucella spp. isolated from human brucellosis in Malaysia using high-resolution melt (HRM) analysis. Diagn Microbiol Infect Dis 81: 227-233.
35. Asaad AM, Alqahtani JM (2012) Serological and molecular diagnosis of human brucellosis in Najran, Southwestern Saudi Arabia. J Infect Public Health 5: 189-194.
36. Al Dahouk S, Neubauer H, Hensel A, Schöneberg I, Nöckler K, Alpers K, Merzenich H, Stark K, Jansen A (2007) Changing epidemiology of human brucellosis, Germany, 1962-2005. Emerg Infect Dis 13: 1895-1900.

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Conflict of interests: No conflict of interests is declared.