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TÍTULO: Características epidemiológicas y la tendencia de incidencia de la brucelosis en el condado de Kohgiluyeh, Irán, periodo 2011-2015.

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RESUMEN: El estudio explora las características epidemiológicas y la incidencia de brucelosis en el condado de Kohgiluyeh en el 2015. El estudio es transversal y analiza 222 individuos con brucelosis (115 hombres y 107 mujeres). Las variables edad, sexo, estación de incidencia, año de incidencia, trabajo, lugar de residencia, historial de consumo de productos lácteos sin pasteurizar, historial de contacto con el ganado en el último año, la afluencia de otros miembros de la familia en los últimos 18 meses y los efectos de la enfermedad se exploraron. Los datos se analizaron utilizando el software SPSS versión 21 y t, prueba de χ^2 . Con la alta tasa de incidencia de brucelosis en la provincia, existe la necesidad de medidas preventivas, especialmente la educación estandarizada en estos grupos.

PALABRAS CLAVES: brucelosis, epidemiología, factores de riesgo, Kohgiluyeh.

TITLE: Epidemiological characteristics and the incidence trend of brucellosis in Kohgiluyeh County, Iran, period: 2011-2015.

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ABSTRACT: This study was conducted with the aim of exploring the epidemiological characteristics and the incidence trend of brucellosis in the county of Kohgiluyeh in 2015. This study is cross-sectional examining the cases of 222 individuals with brucellosis (115 males and 107 females). The variables age, sex, season of incidence, year of incidence, job, place of residence, history of consumption of unpasteurized dairy, history of contact with livestock in the past year, the affliction of other family members in the past 18 month and the effects of the disease were explored. The data were analyzed using the software SPSS version 21 and t, χ^2 test. Considering the high incidence rate for brucellosis in the province, there is a need for preventive measures, especially standardized education in these groups.

KEY WORDS: brucellosis, epidemiology, risk factors, Kohgiluyeh.

INTRODUCTION.

Brucellosis, also known as undulant fever, is the most prevalent infection common between human and livestock and it is transmitted through infected animals and their products. The cause of this disease is a type of gram-negative bacillus known as brucella that is eliminated by pasteurization and boiling but is resistant against coldness and dryness (Kamal et al, 2009). The important species

of this genus include *brucella abortus* and *melitensis* that create most of the disease cases in humans (Hamzavi et al, 2014).

The incubation period of this disease in humans is usually between one and two weeks and rarely a few month (Shoraka et al, 2010). This disease begins acutely and insidiously and emerges with continuous or regular fever with alternate periods, excessive sweating, especially at night, lack of appetite, weight loss, headache, muscle aches and general body pain.

The aforementioned symptoms emerge, depending on the *brucella* type and disease severity, in acute, subacute, chronic and topical forms (Roushan et al, 2004). Mortality due to this disease is rare but, despite the prevalence of this disease, some think that it has been ignored in health systems (Franco et al, 2007; Nuriyev et al, 2018). This disease has different clinical characteristics that challenge the physicians in diagnosis and cause acute and chronic mental and physical disabilities in the individuals afflicted. In addition, this disease has resulted in significant costs for medical organizations in the country (Kamal et al, 2009; Haghshenas et al, 2015).

More than half a million new cases of the disease occur in the world each year that have different distributions in different regions (Soofian et al, 2007). This disease has been taken under control in animals in many developed countries and consequently the disease incidence in humans too has significantly reduced (Hasanzadeh et al, 2013; Parvizian et al, 2015). However, this disease is relatively common in developing countries, especially in the Mediterranean region, Middle East, west Asia and some parts of Africa and America (El-Rab & Kambal, 1998; Moradi et al, 2006).

The disease exists in many developing countries but is not detected in some cases (McDermott & Arimi, 2002; Corbel, 1997). There are nearly four undetected cases for each detected human case. In Iran, similar to many developing countries, there is no accurate information on the yearly incidence of this disease (Hamzavi et al, 2014; Mwaniki & Ondiek, 2018; Tasnim & Farasat, 2018).

Overall, Iran is considered as a country with high prevalence among the countries in the region (Refai, 2002).

According to a report by the World Health Organization, the provinces East Azerbaijan, Hamadan, Lorestan, Markazi, South Khorasan, West Azerbaijan and Kermanshah have a very high infection level (31-41 per 100,000 individuals) and provinces Razavi Khorasan, Kurdistan and Zanzan have a high infection level (21-30 per 100,000 individuals). The disease is seen in both sexes but is slightly higher in males (55.4) than in females (44.6). Occupation is considered as a risk factor, especially in housekeepers, shepherds and farmers. Also, the disease is seen more in spring and summer during the breeding season (Hashtarkhani et al, 2015; Krishtiana & Kimatova, 2015). In addition, the losses due to the elimination of the livestock with this disease are high (Kamal et al, 2009).

In many countries like Iran in which the economic growth and employment are highly dependent on agriculture and animal husbandry brucellosis is considered as the main concern for the economic growth too and its problems are not just limited to human (Kamal et al, 2009). In Iran, surveillance methods are done by epidemiological study of the cases based on the probable case definition, reporting of disease cases monthly and, if necessary, sentinel surveillance of the at-risk groups and the current yearly reports show the disease trend during continuous years and its relation with factors impacting the increase or the decrease of the disease (Nimri, 2003).

In the existing surveillance system for brucellosis in Iran, for data collection, the list of individuals afflicted is collected on weekly basis (during 2011-2015) from the laboratories, physician offices and clinics in the county and sent to the health center of the county. Then, after elimination of the duplicates, the new cases are identified and, finally, as soon as a new case is identified, it is explored by physicians and experts of disease control and prevention at health centers. Afterwards, the treatment process for them is followed and individual forms are completed for them and finally, the

county statistics, after being recorded in the epidemiological study form from 2014, is entered into the portal of the Ministry of Health and Medical Education.

The identification of the patients is based on laboratory diagnosis in which antibody is identified in the patient's serum. An important thing in laboratory diagnosis is proper application of the tests and the use of standard antigens. In addition, the time of serum test is highly important; for example, in the first week of the disease there is no immunoglobulin and consequently the test result is negative.

The experts of the World Health Organization (WHO) and Food and Agriculture Organization (FAO) have recommended five tests with standard antigen methods for serum detection of brucellosis which are: Rose Bengal test, Wright seroagglutination test, 2-mercaptoethanol (2ME) test, Complement Fixation test and antiglobulin coombs. For definite diagnosis of brucellosis in the surveillance system, after clinical suspicion of the diseases, the diagnostic criteria are as follows: 1. Separation of brucella from the clinical sample; 2. 2ME titer of higher than 1.40; and 3. Fourfold or more increase in brucella agglutination titer two weeks after the initial test (Nimri, 2003).

Prevention, control or eradication of brucellosis in a country requires policy making, decision making and having accurate epidemiological statistics and information (Kamal et al, 2009). Considering the significant prevalence of brucellosis in Kohgiluyeh county which is an important center of animal husbandry and livestock production in Iran, it was decided to determine some epidemiological indices of the disease in this county during 2011-2005.

The results of this study can, in addition to, delineate the epidemiological status of the disease in the county, be used in the management of health services for planning for prevention, control or treatment and follow-up of the disease.

DEVELOPMENT.

Materials and methods.

This study is a cross-sectional study that was conducted by examining the medical files of 222 individuals with brucellosis in the county of Kohgiluyeh in 2015. Ethical code No. 251245 was received from Yasuj University of Medical Sciences on August 11, 2011. In the cases of incompleteness of some information, the patients were contacted, and the information was completed. After coding, the data were entered into SPSS version 21. Descriptive statistics of frequency, mean and standard deviation were used for data description. Chi-square test or Fisher exact test is used for exploring the relationship between variables.

Results.

The information on 222 patients with brucellosis for 5 years (2011-2015) was examined. The incidence of brucellosis during 2011-2015 was 6.77, 16.1, 28.35, 50.47 and 28 per 100,000 individuals respectively. The incidence rate of the disease is different in different seasons. According to the explorations, the incidence of the disease is higher in spring and summer, compared with other seasons, in a way that 49.1 percent of the patients were in spring, 28.8 percent were in summer, 12.2 percent were in fall and 9.9 percent were in winter (chart 1).

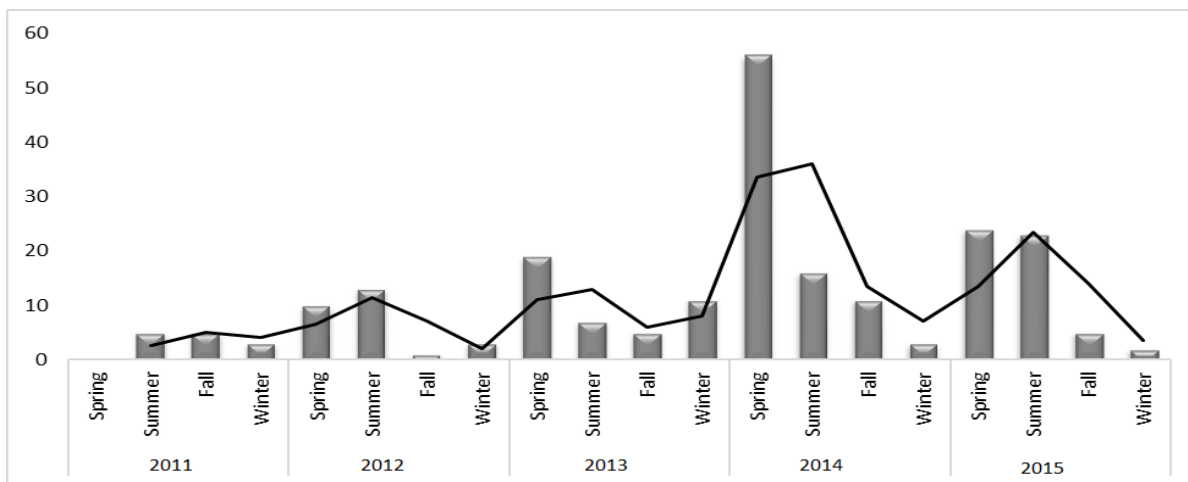


Figure 1. The trend of incidence of Brucellosis in Kohgiluyeh County during 2011-2015.

The disease cases included 107 females (48.2%) and 115 males (51.8%) and the place of residence of most of them (77.9%) was in rural areas. Most of the disease cases have occurred in males (75%) in rural areas. The mean age of the individuals afflicted was 38.5(\pm 17.3) years. The mean ages in rural and urban individuals were 37.8 (\pm 17.2) and 40.9(\pm 17.7) years respectively. The highest frequency (32%) was in individuals at 30-44-year-old group and the lowest frequency (9.9%) was at 0-15-year-old age group. Also, the mean age was 35.5 (\pm 15.9) years in the women and 41.35 (\pm 18.2) years in the men. The cases of the disease in women were observed in lower ages in rural areas and higher ages in urban areas. In terms of occupation, most of the number of incidences of the disease was in farmers (39.9%) and female housekeepers (34.4%) (Table 1).

Table 1. The demographic characteristics of the individuals with brucellosis.

Patients' demographic characteristics	Frequency(percentage)
Age groups	
Lower than 15 years	53(23.9)
15-29 years	53(23.9)
30-44 years	71(32)
44-59 years	51(23)
60 years and higher	25(11.2)
sex	
male	115(58.1)
female	107(48.2)
Place of residence	
Urban	49.(22.1)
Rural	173(77.9)
Occupation	
Animal farmer	88(39.9)
farmer	3(1.4)
Butcher	6(2.7)
employee	5(2.3)
Civil servant	76(34.4)
student	19(8.6)
Self-employed	11(5)
University student	1(0.5)
driver	2(0.9)
worker	2(0.9)
child	5(2.3)
unemployed	3(1.4)

As seen in table 2, about 57.7% of the patients have a history of consumption of unpasteurized dairy, 45.5% of whom have consumed milk as the most common unpasteurized dairy. About 28.3 percent of the patients had a history of contact with livestock in the past year. About 18.5% of the individuals had a history of incidence of the disease in other members of the family in the past 18 years. 0.9% of the patients had been afflicted with the disease in the past and had visited due to the treatment failure.

Most clinical symptoms in the individuals were musculoskeletal pain (90.5%) and fever (81.1%). The most common medicines prescribed were Rifampicin (76.475) and Doxycycline (46.86). About 65.8 percent of the patients underwent treatment with two-drug regimen, 18.9% with three-drug regimen and 15.3% with one-drug regimen. About 43 percent of the three-drug consumers were male and 57.1 percent were female.

Table 2. The distribution of the individuals with brucellosis.

Characteristics explored	Frequency (percentage)
History of consumption of unpasteurized dairy	128(57.7)
Type of the unpasteurized product used	
milk	121(45.5)
cheese	1(0.5)
butter	0(0)
colostrum	4(1.8)
Ice cream	1(0.5)
History of contact with livestock in the past year	63(28.3)
Type of contact with livestock	
Keeping livestock	41(18.5)
Contact with alive livestock	18(1.8)
slaughter	2(0.9)
Contact with livestock discharges	2(0.9)
Affliction of other family members in the past 18 years	41(18.5)
Treatment failure	2(0.9)

Chi-square test was used for exploring the impact of place of residence on brucellosis incidence. The results indicated that the frequency of the individuals with brucellosis observed in city was 49 while it was expected to be 111. In addition, the frequency of the individuals with brucellosis observed in

village was 173 while it was expected to be 111. The results of exploring the impact of place of residence on brucellosis incidence indicated that individuals in villages become afflicted with brucellosis more than those in the city at significance level of 0.05 ($p\text{-value} < 0.0001$).

Chi-square test was used for exploring the impact of sex on brucellosis incidence. The results of the study indicate that the frequency of the women with brucellosis observed was 115 while it was expected to be 111. In addition, the frequency of the men with brucellosis observed was 107 while it was expected to be 111. The results of exploring the impact of sex on brucellosis incidence indicated that no significant difference was seen between men and women in terms of brucellosis incidence at significance level of 0.05 ($p\text{-value} < 0.59$).

Fisher's exact test was used for exploring the impact of occupation on brucellosis incidence. The results of exploring the impact of occupation on brucellosis incidence indicated that there was a significant difference between occupations in terms of brucellosis incidence at significance level of 0.05 ($p\text{-value} < 0.0001$).

Chi-square test was used for exploring the impact of history of consumption of unpasteurized dairy on brucellosis incidence. The results indicated that the frequency of the individuals with brucellosis who reported history of consumption of unpasteurized dairy was 199 while it was expected to be 111. In addition, the frequency of the individuals with brucellosis who reported no history of consumption of unpasteurized dairy was 23 while it was expected to be 111. The results of exploring the impact of history of consumption of unpasteurized dairy on brucellosis incidence indicated that there was a significant difference between individuals in terms of history of consumption of unpasteurized dairy and brucellosis incidence at significance level of 0.05 ($p\text{-value} < 0.0001$).

Chi-square test was used for exploring the impact of age groups on brucellosis incidence. The results indicated that the frequency of the individuals with brucellosis in the under-15 age group was 22 while it was expected to be 44.4. In addition, the frequency of the individuals with brucellosis in the

15-29-year-old age group was 46 while it was expected to be 44.4. The frequency of the individuals with brucellosis in the 30-44-year-old age group was 70 while it was expected to be 44.4. The frequency of the individuals with brucellosis in the 45-59-year-old age group was 56 while it was expected to be 44.4. The frequency of the individuals with brucellosis in the over-60 year-old age group was 28 while it was expected to be 44.4. The results of exploring the impact of age group on brucellosis incidence indicated that there was a significance difference between age groups in terms of brucellosis incidence at significance level of 0.05 ($p\text{-value} < 0.0001$).

Chi-square test was used for exploring the impact of season on brucellosis incidence. The results of exploring the impact of season on brucellosis incidence indicated that there was difference between seasons and brucellosis incidence at significance level of 0.05 ($p\text{-value} < 0.0001$).

Discussion.

The incidence of brucellosis and the factors impacting this disease in Kohgiluyeh county (Kohgiluyeh and Boyer-Ahmad Province) were explored in this study. According to the results of the present study, the annual incidence of the disease in Kohgiluyeh county is about 25.9 per 100,000 individuals and, based on the categorization of the Ministry of Health in 2012, this county is among the regions with high infection (incidence of 21-30 per 100,000 individuals) (Hashtarkhani et al, 2015). It should be noted that the incidence is based on the number of disease cases identified and reported to the health center of Kohgiluyeh county, and as many cases of the disease may remain undetected, the real incidence statistic in the county is probably higher and this makes the county one of the regions with very high infection rate (incidence of 31-41 per 100,000). It is estimated that, even in developed countries in the world, only 4-10 percent of the cases of brucellosis are diagnosed and overall, it seems that the number of the disease cases reported in the world is 10-20 times lower than the real number of the disease cases (Kasper, 2005).

According to the information obtained, the incidence of brucellosis in this county has been increasing from 2011 to 2014 and decreasing in 2015. The increasing trend of the disease till 2014 may be due to the lack of vaccination of livestock by the veterinary department, the lack of brucella vaccine in country in recent years, illegal importation of livestock to the county and the lack of healthy animal slaughter. And the decreasing trend in the incidence of the disease in 2005 in this county which was accompanied with the decreasing trend in the incidence of the disease in the country can be due to the education of the target groups based on SHEP¹ model and with priority at villages, education of village representatives in the country and the increase of livestock health and vaccination.

The results of the present study indicated that the highest number of the disease cases occur in men and this finding is consistent with the results of other studies conducted in Iran and abroad (Shoraka et al, 2010; Moradi et al, 2006; Hashtarkhani et al, 2015; Mirzaei, 2017). The female to male ratio in the present study was 1.07 to 1 and in the study by Esmailnasab et al in Kurdistan was 1.02. In a similar study by Soleimani in East Azerbaijan province men accounted for 54.9 percent of the cases and women 45.1 percent of the cases (Dastjerdi et al, 2012).

The results of studies have indicated that in endemic areas the highest number of brucellosis cases is in young men (Shoraka et al, 2010; Moradi et al, 2006; Hashtarkhani et al, 2015; Dastjerdi et al, 2012; Kumar et al, 2019). In the study by Gur et al in Turkey the ratio of males to females was 1.05 to 1 (Moradi et al, 2006⁹) and in the study by Serra Alvarez et al in Spain men were 4 times more afflicted than women (Serra & Godoy, 2000). However, in some other studies, the incidence cases have been higher in women than in men; for example, in Isfahan the ratio of female to male patients was higher than 2 (Dastjerdi et al, 2012). In addition, the results of the present study indicated that the highest number of disease cases was in males in rural areas (75%) due to direct contact with alive livestock, keeping livestock, slaughtering livestock or contact with livestock discharges, presence in

¹ Systematic comprehensive Health Education and promotion.

the places in which livestock is kept, contact with manure and consumption of unpasteurized and unboiled dairy.

As in the rural areas of Kohgiluyeh county usually a significant part of the livestock and dairy production such as feeding and farming, milking, cleaning the barns and stalls and production of dairy is done by female housekeepers, it is possible that the ratio of the disease incidence will increase in women compared with men. Therefore, it is necessary to pay attention to educational programs for prevention of brucellosis in human and education of livestock health in this group.

In this study, it was found that some of those afflicted had a history of the disease in their family members and it can be due to the contact of the family members with infected livestock or due to the consumption of infected dairy in the family. Due to the contacts the individual can have with infected livestock, the contact has been considered as a factor related to the disease. In terms of job, the highest number of cases belonged to the livestock producers, female housekeepers and students. The cases of the disease were more in rural students than in urban students as the use of unpasteurized dairy is higher in students in villages than those in cities.

In this study, most of the individuals with the disease were living in village. In the study by Esmailnasab et al in Kurdistan 90 percent of the patients were in villages (Esmailnasab et al, 2007). 63% of the patient in the Saudi Arabia (Esmailnasab et al, 2007), 58.7% in Turkey (Serra & Godoy, 2000) and 60.8% in Babol (Moradi et al, 20069) were living in village. This can be expected because the rural individuals are usually farmers and livestock producers and their contact with livestock, especially during breeding, is high. They also use unpasteurized dairy, especially milk, more, compared with the city and livestock production in Iran is still done in the highly traditional style. Also, it seems that urban people use pasteurized yogurt and cheese.

The most common clinical symptoms were musculoskeletal pain and fever. Other symptoms in patients were weakness, lack of appetite, weight loss and spleen enlargement. In a similar study in Arak, fever, muscle pain and chills were the most common symptoms in patients (Soofian et al, 2007).

The disease was seen more in the 30-33-year-old age group. In a study by Moradi et al in Kurdistan, the highest number of the disease cases were in 50-59-year-old (63.3%) and 30-39 year-old (58.3%) age groups (3). In the present study women's mean age was 5 years lower than the men's mean age which is consistent with the results of the study by Farazi et al conducted in Arak in which the mean age in men was 1 year higher than the mean age in women (Farazi et al, 2014; Sakthi Priya et al, 2017).

The results of the present study showed a significant difference in age of incidence in urban and rural women in a way that the incidence cases was seen more in younger women in rural areas due to contact with livestock and milking and, in urban areas, due to the consumption of unpasteurized dairy, the cases were seen more in older women. Overall, the under-40 age group which is the active group in the society in terms of occupation showed the highest number of the disease cases (Dastjerdi et al, 2012). As the highest number of the cases is in the age group that are economically productive and active, the necessity of education and prevention of the disease for the prevention of its problems needs to be a priority of educational programs in all age groups and especially in this age group.

The results of the study indicated that the lowest number of the brucellosis cases happened in fall and winter and the highest number of cases happened in spring and summer and these results are consistent with those of other studies (Roushan et al, 2004; Dastjerdi et al, 2012; Hakiminya & Parnian, 2018; Alton et al, 1975). In the study by Esmailnasab et al in Kurdistan the highest number of the cases diagnosed were reported in spring and early summer (the highest number of cases were

seen in April, June and July and the lowest number of the cases were seen in October and January (Esmailnasab et al, 2007).

As spring and summer are the seasons in which livestock produce the highest amount of milk and the production of dairy and contact with livestock are more in these seasons, most of the disease cases are seen in these seasons. Also, as the highest number of the disease cases are in rural areas in spring and summer which are the seasons for breeding, milking and dairy production, there is a necessity for standard education based on Shep model in villages before these seasons including the conditions for milk boiling, voidance of direct contact with newly-born livestock during birth and observance of livestock health.

CONCLUSIONS.

Considering the results, it seems that brucellosis is one of the diseases with a high incidence in the Kohgiluyeh county and its incidence is higher in this country than many other parts of the country. Despite long-term programs for fighting this disease, it is still one of the common diseases.

Some of the reasons for this condition is the development of livestock and dairy production without using scientific and modern methods, continuation of traditional animal husbandry, traditional dietary habits, lack of enough knowledge on individual and environmental health, the lack of standard methods for collection and preparation of milk, non-standard transportation of animals and lack of complete vaccination coverage against the disease in livestock.

Necessary education based on standard methods should be provided especially to young individuals and high-risk occupational groups. In addition, healthy behaviors contributing to the prevention of the disease including avoiding consuming unpasteurized dairy, coordination for livestock vaccination and knowledge of the disease symptoms for treatment should be employed in appropriate time.

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