

## BRUCELLOSIS IN IRAN: THE FARS PROVINCE EXPERIENCE

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### ABSTRACT

Over a 10-year period, 130 consecutive cases of brucellosis were encountered and were prospectively treated and followed. Twenty-one cases were children and the remainder were adults. There were 93 males and 37 females with a male: female ratio of 2.5 to one. The age range of the patients was from 2 to 74 years with a mean of 30 years. Fifty-five percent of cases were from rural areas and the rest from major cities of the Fars province. The disease was most frequently seen during spring and summer. Although it was seen in ranchers and farmers who usually deal with small ruminants in our country, it was also frequently seen in those with other professions. Animal contact was common (33%) as well as consumption of raw unpasteurized milk and fresh cheese which was seen in almost half of the cases. Fever and sweating were the most common complaints and arthritis and splenomegaly were the most frequent physical findings. Bilateral sacroiliac joint involvement was the most common arthritic disorder and was exclusively seen in adults. Knee and ankle joint involvement was commonly seen in children. They were unilateral and monoarticular in their presentation. Seven cases had orchitis and one pregnant lady developed second trimester abortion. Treatment with conventionally recommended antibiotics was successful in all except two cases who had relapse secondary to an inadequate course of drug therapy. The two, however, responded to another course of full term antibiotic therapy with full recovery.

In contrast to western countries where cattle and swine are the most frequent sources for human brucellosis, sheep and goats are the most common source of infection in our country. Here, the disease is not an exclusively occupational one for young adult males and an indirect oral route of disease transmission is quite frequent. Brucellosis, therefore, affects both children and adults of either sex, with a wide age range. Prohibition of ingestion of raw milk and fresh cheese as well as control of *Brucella melitensis* infection in sheep and goats can significantly reduce the burden of disease in our country.

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### INTRODUCTION

Brucellosis continues to be an ongoing, world-wide

public health problem both for humans and animals.<sup>1</sup> Although the incidence of this disease varies from one geographic area to another, the middle east and the mediterranean regions are two of the most heavily affected.<sup>1-4</sup> The disease is incapacitating in its acute form

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and if untreated, may become chronic with recurrent acute episodes and debilitating complications.<sup>5-7</sup> It is endemic in Iran, and the Fars province is not an exception.<sup>8-10</sup> It is common among domestic farm animals, especially sheep and goats.<sup>10</sup> Human brucellosis is usually characterized by fever and a series of protean clinical manifestations which partly depend on the duration of the disease. Here we report our experience with 130 documented cases of acute and subacute untreated brucellosis in Fars province.

### PATIENTS AND METHODS

During a ten-year period, 180 consecutive cases who were highly suspected to have brucellosis were referred to our "Brucella Clinic" in Shahid Faghihi Hospital, affiliated to Shiraz University of Medical Sciences. All patients had a thorough medical interview, physical examination, and serologic tests for brucellosis. The tests included rose bengal plate agglutination (RB); standard tube agglutination test (SAT) and 2-mercapto-ethanol agglutination test (2-ME).<sup>11</sup> Bone marrow and/or blood cultures were not done. The diagnosis of brucellosis was made when a rise in antibody titer of four-fold or greater was found or when a single titer of > 1: 160 was found for 2-ME in the presence of symptoms and signs com-

patible with the disease. Fifty cases who were partially treated and/or those who didn't meet the above criteria were excluded from the study. Documented cases were treated within a pre-set treatment protocol with tetracycline plus streptomycin, trimethoprim-sulfamethoxazole or rifampin plus tetracycline.<sup>12-14</sup>

Treatment was continued for  $\geq 4-8$  weeks until there was an improvement in symptoms and a 4-fold decline in serologic titers. All treated patients were asked to have regular weekly follow-ups and serologic studies. Once clinical and serologic improvement was evident, cases were visited every 3-4 weeks and as needed thereafter.

### RESULTS

Of the remaining 130 cases with acute and subacute untreated brucellosis, there were 93 (61%) males and 37 (39%) females, with a male: female ratio of 2.5 to one. Twenty-one cases were children. The age of the patients ranged from 2 to 74 years, with a mean age of 30 years. The majority of cases (56%) however were between 5-39 years of age. Fifty-five percent of patients were from rural areas and the remainder from major cities of the Fars province, mainly the city of Shiraz. The symptoms and signs of the cases are shown in Table I and II respectively. The onset of symptoms occurred predominantly

**Table I.** The presenting symptoms in 130 consecutive cases of brucellosis in Fars province Iran.

Symptoms	Children (N= 21)*		Adults (N= 109)*		Total (N= 130)	
	Number	%	Number	%	Number	%
Fever	19	90	109	100	128	98
Sweating	15	71	104	95	119	92
Weakness	16	76	89	82	105	81
Chills	12	57	90	83	102	78
Arthralgia	19	90	75	69	94	72
Headache	10	48	83	76	93	72
Weight loss	8	38	76	70	84	65
Anorexia	11	52	70	64	81	62
Low back pain	9	43	67	61	76	58
Malaise	8	38	48	44	56	43
Irritability	6	29	50	46	56	43
Cough	4	19	30	28	34	26
Abdominal pain	6	29	28	26	34	26
Constipation	4	19	27	25	31	24
Vomiting	2	10	23	21	25	19
Dysuria	1	5	19	17	20	15
Testicular pain	0	0	12	11	12	9
Diarrhea	0	0	9	8	9	7
Abortion	0	0	1	1	1	1
Jaundice	0	0	0	0	0	0

N\*: Total number of patients in each age group.

**Table II.** Clinical findings in 130 consecutive cases of brucellosis in Fars province, Iran.

Signs	Children (N= 21)*		Adults (N= 109)*		Total (N= 130)	
	Number	%	Number	%	Number	%
Arthritis	10	48	48	44	58	45
Splenomegaly	10	48	47	43	57	44
Tender Spine	4	19	33	30	37	28
Hepatomegaly	4	19	21	19	25	19
Lymphadenopathy	5	24	12	11	17	13
Orchitis	0	0	7	0	7	5

N\*: Total number of patients in each age group.

in the spring and summer, although sporadic cases were seen throughout the year. Over 28% of patients were ranchers and farmers, however the disease was equally frequent in housewives and to a lesser extent in students. The most probable source of infection was contact with small ruminants, namely sheep and goats; such a history was present in 58.5% of our cases.

In addition, 33% of cases had a history of contact with animals who had a recent abortion. Unpasteurized dairy products, primarily raw milk and fresh cheese were implicated in 49% of our patients. The mean duration of clinical follow-up after termination of therapy was 24 weeks with a range of 2-199 weeks. No fatalities were seen, but 2 patients had relapse during follow up.

## DISCUSSION

Brucellosis remains a major zoonosis world-wide.<sup>15,16</sup> In western countries cattle and swine are the most frequent sources from which humans may be infected<sup>17,18</sup> and the disease is often that of adult males who have occupational exposure to livestock.<sup>19</sup> A changing pattern toward ingestion of unpasteurized goat milk, however, has recently been noted in the United States.<sup>18</sup> Animal contact with sheep and goats however, was the most probable source of infection in our cases (58%). The absence of such a history in over 40% of the remaining patients however indicates the importance of the indirect method of disease transmission in our population.<sup>20</sup> Consumption of unpasteurized dairy products, as was found in half of our cases, has previously been shown to be a potentially important source of human brucellosis in urban areas, although both direct and indirect transmission may occur in rural areas.<sup>10,21,23</sup> The disease is not rare in children as once thought, especially in countries where *Brucella melitensis* is enzootic,<sup>24,25</sup> and our region is no exception.<sup>8,10</sup> Although in the present study about 14% of the cases were children, since bone marrow and/or blood cultures were not done, we couldn't make a definite state-

ment regarding the exact species of the causative brucella organism(s).

There were two families whose members had brucellosis all at once. This kind of outbreak happens because a common food source is usually involved.<sup>26,27</sup> The symptoms of brucellosis are nonspecific and may be misleading.<sup>28</sup> The most common symptoms were fever and sweating in our series. Adults were more symptomatic than children but joint pain was more common among the latter group. The signs and symptoms of our cases were somewhat similar to those previously reported.<sup>3,28</sup> Arthritis was the most frequent physical finding (45%) and the sacroiliac joint was most frequently involved. It was bilateral in almost 50% of cases and was exclusively seen in adults. Peripheral joint involvement including the knee and ankle, however, was more common in children. They were mainly unilateral and monoarticular. Similar results have been reported from Kuwait.<sup>4</sup> Splenomegaly was next in frequency (44%). Its prevalence was higher than that reported from Kuwait,<sup>30,31</sup> but similar to that of Saudi Arabia.<sup>3</sup> Orchitis is a rare complication of brucellosis and is usually unilateral.<sup>32</sup> This was exclusively present in a few of our adult male patients, 3 of whom had epididymitis as well. None of the children had testicular pain either. Whether the presence of sperm in the testes plays a precipitating role is to be clarified. Brucellosis is a well known disease causing abortion in animals.<sup>33</sup> Although isolated cases have been reported in humans,<sup>34</sup> and one of our cases had a second-trimester abortion too, the role of brucellosis in this matter needs further clarification. All therapeutic modalities used were effective and only 2 episodes of relapse were noted which were secondary to inadequate duration of therapy and both cases recovered following continuation of their antibiotic regimens.<sup>35</sup>

## CONCLUSION

Brucellosis is a preventable disease and its prevention in man is dependent on control of the disease in animals. Animal brucellosis has been successfully eradicated

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in some European countries<sup>36</sup> while in others attempts to control the infection have been focused around the vaccination of young animals and slaughtering older ones with serologic evidence of the disease.<sup>37</sup> However despite widespread vaccination of young animals with the Rev 1 strain, *Brucella melitensis* remains the principal cause of human brucellosis. Unfortunately there is yet no satisfactory vaccine against human brucellosis although attenuated pure E mutants have shown to be promising.<sup>38</sup> In brief, in order to decrease the incidence of human brucellosis in our country, all possible efforts should be made to control *Brucella melitensis* infection in goats and sheep. This can be achieved by use of newly developed vaccines and by promoting public education to ban the consumption of unpasteurized dairy products.

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