Brucellosis remains one of the world’s principal zoonotic infections that constitute a major public health problem and economic burden in many parts of the world, in particular, Saudi Arabia. Many factors have been implicated in the transmission of Brucellosis and its prevalence in Saudi Arabia, such as the social customs, dietary habits of its people, uncontrolled importation of poorly screened animals, lack of legislation for proper control of the marketing and movement of animals, husbandry practices, poor animal quarantine procedures and poor cooperation and exchange of information between veterinary and health services. The growing population of Saudi Arabia with its increased demand for dairy products accompanied with changing and intensified farming practices raises the concern for further spread and perpetuation of this disease. The eradication of human brucellosis in Saudi Arabia ultimately depend on the eradication of animal brucellosis. An effective national brucellosis control programme is therefore required.

This paper describes the history of brucellosis and the current public health picture in Saudi Arabia. It aims to highlight the current epidemiological situation, identify trends and possible risk factors for Brucellosis and barriers to its control and prevention in Saudi Arabia. A current case report of brucellosis was given.

Key Words: Brucella spp – Brucellosis – Human brucellosis – Epidemiology – Surveillance – Control – Saudi Arabia.

Introduction

BRUCELLOSIS is one of the world's major zoonotic infections that remain of public health and economic concern in many parts of the world.

Brucellosis is caused by bacteria (small, fastidious gram negative coccobacilli), of the genus Brucella. There are four important species pathogenic to humans: Brucella melitensis, found primarily in goats, sheep and camels; Brucella abortus in cows; Brucella suis in pigs and Brucella canis in dogs. The Brucella species differ in degree of virulence and invasiveness. B. melitensis is the most invasive and produces the most severe disease. B. abortus is the least invasive and causes the mildest illness. Currently B. melitensis remains the principal cause of human brucellosis worldwide, including Saudi Arabia [1].

Brucellosis has a worldwide distribution; but currently the disease incidence has become rare amongst most industrialized countries because of routine screening of domestic livestock, implementation of effective animal vaccination programmes and strict regulations regarding animal importation and other precautionary measures. However, Brucellosis remains a leading zoonosis in the developing countries of the Eastern Mediterranean Region [2].

It is primarily a contagious disease of domestic animals-goats, sheep, cows, camels and dogs. Brucella organisms are shed in their milk, urine and vaginal discharges. Sheep and goats and their products are the main sources of infection. Inter-human transmission of brucellosis has been rarely reported [3]. As a result brucellosis has been an occupational risk e.g., among shepherds, farmers and veterinarians, and through inhalation of infectious aerosols (e.g., by workers in abattoirs, animal husbandry personnel and microbiology laboratories). Non-occupational sources of infection include consumption of un-pasteurized milk, goat cheese and raw meat [4].

Eradication of brucellosis in animals is the key to prevention in humans. Therefore, the transmission of Brucella infection and its prevalence in a region depends upon several factors like social customs and dietary habits of its people, methods of processing dairy products, husbandry practices,
climatic conditions, socio-economic status and environmental hygiene. Environmental sanitation is particularly important in the context of air borne transmission [9].

Brucellosis is almost invariably transmitted to man from infected domestic animals. However, the possibility of human to human transmission of Brucella infection has also been reported in the literature [5,12]. Breast milk has been implicated as a source of transmission of Brucellosis from mothers to their young infants [9,10,11].

Dairy products prepared from unpasteurized milk such as soft cheese, yoghurts and ice-creams may contain high concentration of the bacteria and consumption of these is an important cause of brucellosis [5,12]. It is the commonest mode of transmission in case of B. melitensis and B. abortus infections in general population. Camel milk is also considered to be the important source of infection in Middle East countries. Bacterial load in animal muscle tissues is low, but consumption of undercooked traditional delicacies such as liver has been implicated in human infection [13].

Historical perspective: [5]

Brucellosis has many synonyms derived from the geographical regions in which the disease occurs e.g., Mediterranean fever, Malta fever, Gibraltar fever, Cyprus fever; or from the remittent character of the fever e.g., Undulant fever; or from its resemblance to malaria and typhoid e.g., Typhomarial fever, Intermittent typhoid.

Brucellosis is characterized by its type of fever, with its regular remissions or intermissions and its occurrence has been documented along the Mediterranean littoral since the time of Hippocrates in 450 B.C.

In the 19th century, the disease was noted to have affected the British troops and the local population of Malta. In 1861, Marston, a British surgeon working in the Mediterranean at the time, first described the symptoms of brucellosis as, "gastric remittent fever".

The cause of this disease was obscure until 1887 when Sir David Bruce - a Scottish physician reported numerous small coccoid organisms in stained sections of spleen from a fatally infected soldier. He isolated and identified the same organism from cultures obtained from the spleen tissue of four other affected British soldiers stationed at Malta. This organism, which he designated Micrococcus melitensis, produced a remittent fever in inoculated monkeys. One animal died from the infection and the organism was recovered in pure culture from the liver and spleen. The organism derived its species name from Melita (honey), the Roman name for the Isle of Malta.

Hughes in a monograph in 1897 portrayed the findings in people in greater detail, emphasizing "undulant fever" and suggested the name undulant fever. In 1897, Wright and Smith detected antibodies to M. melitensis in human and animal sera through agglutination test, and in 1905 Zammit a young Maltese physician working with Mediterranean Fever Commission confirmed it by isolating the organism from the milk and urine of goats. While in Denmark gram-negative rod were isolated from cattle, which had aborted. A third type, also bacillary in shape, was recovered from the foetus of aborted swine by Traum in 1914 in the United States of America and implicated as an agent of brucellosis in man by Huddleson in 1943.

In 1918, Alice Evans an American bacteriologist published reports which contained convincing evidence that M. melitensis from goats and a gram-negative rod from cows could not be differentiated morphologically or by their cultural and biochemical reactions but there were antigenic differences which could be shown by agglutination absorption test. She also showed in 1920 that M. melitensis was also a bacillus. She showed that M. melitensis, isolates of cows and pigs belonged to one genus, and suggested the possible pathogenicity of B. abortus to man. Meyer and Shaw further confirmed Evan’s observations and suggested the generic name Brucella in honour of Sir David Bruce. In 1956, Buddle and Boyce discovered B. ovis, the cause of epididymitis in rams. In 1957, Stoennner and Lackman isolated B. neotomae from desert wood rat in Utah in the USA. In 1968, Carmicheal and Bruner discovered B. canis as the cause of an epidemic of abortions in beagles. Human infections due to B. canis have been reported [14]. Two new Brucella species, provisionally called B. pinnipe-diae and B. cetaceae have been isolated from marine hosts within the past few years [15,16]. There are three reports in the literature of humans infected with marine mammal strains of Brucella; one infection occurred in a research laboratory worker after occupational exposure [17] and the other two were community-acquired infections, including the recent report in a patient of New Zealand with spinal osteomyelitis [18,19].

Epidemiology:

The epidemiology of brucellosis is complex and it changes from time to time. Wide host range and resistance of Brucellae to environment and
host immune system facilitate its survival in the populations.

Global scenario:

Worldwide, brucellosis remains a major source of disease in humans and domesticated animals. The disease is endemic especially in countries of the Mediterranean basin, the Arabian Gulf, the Indian subcontinent and parts of Mexico and Central and South America. Human brucellosis is found to have significant presence in rural/nomadic communities where people live in close association with animals. The true incidence of human brucellosis however, is unknown for most countries. Worldwide, reported incidence of human brucellosis in endemic disease areas varies widely, from less than 1 per 100 000 to more than 200 per 100 000 population. Official figures do not usually fully reflect the real magnitude in humans. It is estimated that the actual incidence may be up to 25 times higher than the reported incidence due to misdiagnosis and underreporting [20].

Recent re-emergence in Malta and Oman indicates the difficulty of eradicating this infection. Sheep and goats and their products remain the main source of infection, but B. melitensis in cattle has emerged as an important problem in Saudi Arabia as well as some southern European countries, Israel and Kuwait [20].

In some South American countries, particularly Brazil and Colombia B. suis biovar 1 has become established in cattle [21]. In some areas, cattle are now more important than pigs as a source of human infection.

The recent isolation of distinctive strains of Brucella from marine mammals [15,16] as well as humans [17,18,19] has extended the ecological range of human brucellosis. Because new strains may emerge and existing types adapt to changing social and agricultural practices, the picture remains incomplete.

Brucellosis in Saudi Arabia:

Although sporadic human cases of brucellosis were reported between 1956 and 1982 in Saudi Arabia [22] it was not until the early 1980s that the disease emerged as a major public health problem of almost epidemic proportions [23-27]. Despite its control in many developed countries the disease remains endemic in Saudi Arabia where the national seroprevalence of the disease is 15% [3,28].

The prevalence of human brucellosis correlates closely with the extent of animal infection in a given country. For the annual pilgrimage (Hajj) season rituals, the Kingdom is obligated to import millions of sheep for sacrifice. Imported animals come from Africa, India and Australia. In the late 1970s, during the Saudi economic boom, the government began sponsoring the development of dairy farms, sheep and cattle breeding projects and trade with minimal veterinary resources. This led to the uncontrolled importation of animals that were poorly screened for infection and subsequent introduction of brucellosis into the Kingdom [29].

Sero-epidemiologic surveys carried out on imported and local animals for brucellosis, during annual pilgrimage (Hajj) season 1977, revealed higher incidences of infection among imported animals [24].

In the 1980s, the increased rates of annual admissions for brucellosis were observed in the large tertiary care hospitals [30-35]. This rise in incidence of human brucellosis correlated well with the steady increase in the incidence of Brucella infection amongst the livestock in Saudi Arabia.

The incidence of brucellosis in goats in Mecca region (comparable to rates in other parts of the Kingdom) during 1977 was found to be 0.8%, in sheep 0.5%, in camels 2.8% and in cows 3.6% [24]. By 1987, the incidence of brucellosis had gone up to 18.2% in goats, 12.3% in sheep, 22.6% in camels and 15.5% in cows in the Asir region [36]. This rise in incidence of brucellosis was explained by the uncontrolled importation of potentially infected animals at the time, widespread animal husbandry and the prevailing habit of ingesting raw dairy products, obtained mainly from infected goats or camels, among the population of nomadic background.

Saudi Arabia and some of the neighbouring countries, experienced a considerable rise in number of brucellosis cases during 1991 [36]. This could be explained as either a true brucellosis epidemic or a false increase because of improved diagnostic measures and more meticulous notification. In fact, the number reported was probably much lower than the actual figure as under-diagnosis and under-reporting of cases is a recognized problem in many developing countries. It has been estimated that for each reported case, there are at least 2 additional cases that are not reported or not diagnosed.

In a 1999 report on Brucellosis in the Middle East by the World Health Organization (WHO) and Food and Agriculture Organization (FAO) of the United Nations revealed that Saudi Arabia has the highest incidence of human brucellosis in the region (Graph 1) [37].
Brucella melitensis remains the principle cause of human brucellosis in Saudi Arabia (88-93% of cases) and less frequently B. abortus [23,34,36,38]. The natural reservoir of brucellosis is in domestic animals and animal-to-animal transmission is usually venereal or by ingestion of infected tissue or milk.

Recent national statistics indicate that the disease incidence in humans is close to 40 cases per 100,000. Morbidity in humans in the Saudi population continues to be reported with increasing frequency from various regions of the country, particularly from the rural areas, where traditional Bedouin pastoralist groups reside and human infection is in the range of 1.6%-2.6% [39,40,41]. The disease presents in both sexes and in all ages. However, the age group most commonly affected with Brucellosis in Saudi Arabia was found to be between 15-50 years (mean age 33.8, SD 13.9, years) [42,43]. Brucellosis is predominately an occupational disease, so it would be expected that this age group would be the most affected, having been exposed longer to risk factors related to their occupation.

Males are affected more than females (2:1). This sex distribution in the incidence of brucellosis infection may be because males are more concerned in activities such as slaughter and handling of carcasses and as a consequence they are at greater risk of exposure to infection. In both children (0-14 years) and adults, the disease was more prevalent among males. Male children in the areas studied may be exposed to the same risk factors as male adults. Other studies have, however, observed that the incidence of infection was greater in females than males (or roughly equal) [44,45] in the study areas, those milking the cows and thus having a higher chance of contact and acquiring infection, were mainly females.

The onset of symptoms shows a seasonal pattern with high incidence in spring followed by summer [46,47,48]. The increase is believed to be linked to the delivery (parturition) season of sheep and goats where there is a greater possibility for direct contact with vaginal discharge, foetuses and placentas, which may play a major role in increasing risk of exposure to infection.

Studies were undertaken in residents of the Riyadh and Al Kharj regions in central Saudi Arabia to provide the first reported estimate of the incidence and specific aetiology of human brucellosis in Saudi Arabia [49].

Results revealed that Brucellosis was more common amongst Saudi nationals than expatriates. Among Saudi nationals the study demonstrated a remarkable increase in brucellosis with increasing age and a higher incidence amongst women than men in some age groups. Greatest risk was found to be associated with indirect contact with animals (the consumption of unpasteurized dairy products), as opposed to direct contact with animals. Greatest risk was associated with the consumption of milk and laban (buttermilk), as opposed to cheese or uncooked meats. A greater risk with products derived from sheep and goats rather than camels.
or cattle. When direct contact with animals was considered, the study found a very high risk associated with assisting in animal parturition, but no significant risk associated with other direct (unspecified) animal contact. There was a seasonal fluctuation in the occurrence of brucellosis with the largest number of cases occurring in spring and summer.

The prevalence of brucellosis among abattoir workers in Saudi Arabia was determined through a randomized multi-stage sampling of 1200 abattoir workers. Diagnosis was made by both blood culture and standard tube agglutination test. The overall prevalence of brucellosis was 4.0% among abattoir workers. Infection was more common among butchers (8.9%), veterinarians and veterinary assistants (5.4%) and administrative personnel (1.1%) [50].

As part of nationwide surveys done to assess the prevalence of brucellosis in the south region of Saudi Arabia, it was found that the most important common factors associated with brucellosis included consumption of raw products of animal origin, close contact with domestic animals and the slaughtering and disposal of animal wastes.

Illiteracy, ignorance and the harmful traditional customs fostered by the nomadic heritage and dietary habits of the people form the main barriers to the control and prevention of brucellosis in the community [51].

Isolated reports of brucellosis among family members have been documented. A number of studies have been conducted to determine whether active serological screening of the households' members of acute brucellosis cases would detect additional unrecognized cases or not. All the results confirm that screening family members of an index case of acute brucellosis will detect additional cases [52,53].

A study was undertaken to estimate the prevalence of Brucellosis in patients attending the Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia. The result of 1733 patient's sera tested showed that 153 (8.8%) were positive. Of these, 19 had titre greater than 5120. Two hundred and fifty five patients (14.7%) had titres ranging from 20 to 80. The prevalence of brucellosis in the patients studied by serological tests is 8.8% and indicates that improved control measures are required in the Kingdom of Saudi Arabia [54].

Several studies have been conducted in the region directed towards improving diagnosis of human brucellosis and identifying the epidemiological situation. The results of such studies in Saudi Arabia and other nearby countries in the region, including: Egypt, Jordan, Lebanon, Oman and Sudan, all help to show the impact of brucellosis and the need for a collaborative effort to tackle this emerging public health problem [55].

Case Reports

Brucellosis in endemic and non-endemic regions remains a diagnostic puzzle due to misleading non-specific manifestations and increasing unusual presentations. Fewer than 10% of human cases of brucellosis may be clinically recognized and treated or reported.

In January 21st, 2008, a 14 year old Saudi male patient was admitted into Dr Erfan & Bagedo General Hospital with a history of high grade fever (≥39°C) for further evaluation and management. The patient had been experiencing bouts of high grade fever for 5 days prior to admission, associated with fatigue, generalized muscle and bony aches, nausea and loss of appetite. No other associated symptoms.

No previous history of similar attacks or contact with animals, no history of travel, or consumption of un-pasteurized or untreated milk and other dairy products.

Vital signs were normal except for a temperature of 39°C. His physical examination was otherwise normal.

On investigation the laboratory tests showed the following values: WBC 4.9/cmm (4.8-10.8/cmm) with normal differential, Hemoglobin 13.9g/dl (14.0-18.5g/dl), MCV 79.4 fl (81-99 fl), Platelet count 375/cmm (130-400cmm). Erythrocyte sedimentation rate (ESR) 23mm/h (0-10mm/hr), CRP 2.80 (0-0.5mg/dL). Creatinine 0.7mg/dl (0.7-1.2mg/dl).

Liver function tests showed the following values: Aspartate aminotransferase, (AST) 43 U/L (15-37 U/L); alanine aminotransferase, (ALT) 45 U/L (10-40 U/L).

On further investigation it was found that the patient’s father had been recently diagnosed with Brucellosis on December 3rd, 2007. The father of the patient had been having similar symptoms for more than one month prior to his son’s admission and had been seen at another hospital where he was diagnosed with Brucellosis and was receiving treatment.
Specific investigations including serology and blood cultures for brucella was positive B. Melitensis (1:320) and B. Abortus (1:320) agglutination brucella antibody titers. No other significant findings on investigation.

Appropriate antimicrobial therapy was initiated promptly. He was discharged from the hospital in good condition 5 days after admission and the initiation of treatment, to be followed-up in OPD.

The family members reported no history of any risk factors for Brucella exposure. There is no family history of any direct contact with infected animals or ingestion of un-pasteurized milk and dairy products, nor history of recent travel. However, the father confirmed that a few of the neighbours had been having similar complaints. On further inquiry the only common factor identified between family and the neighbours, was that they had all recently bought cheese from same source-American imported processed cheese from a large central supermarket in Jeddah, Saudi Arabia.

The rest of the family members were brought in for investigation. The family of 4 children (including the patient), the mother and the maid working for the family, were all screened.

The second admission was the brother of the above patient, a 2 years and 7 months old baby boy, admitted with intermittent fever and right side hip pain on 26/1/2008. The baby boy was breast fed and also on formula milk. On examination patient generally well, temperature 39.5°C. With family history of brucellosis the family were screened for brucella, investigations revealed a positive agglutination test for brucellosis at a titer-Brucella Abortus 1:320, Brucella Mellitensis 1:320 initially and repeat tests showed rise in titres-Brucella Abortus 1:640, Brucella Mellitensis 1:640.

On investigation the laboratory tests showed the following values: WBC 7.0/cmm (4.8-10.8/cmm), lymphocytosis 67.4% (20.5-51.1%) & monocytes 9.0% (1.7-9.3%), neutrophils 20.3% (42.2-75.2%), Hemoglobin 12.2g/dl (14.0-18.0g/dl), MCV 69.8 fl (80-94 fl), Platelet count 372/cmm (130-400cmm). Rising ESR up to 60mm/hr (0-10mm/hr), CRP 4.8 (0-0.5mg/dL). Creatinine 0.3mg/dl (0.7-1.2mg/dL).

Liver function tests showed the following values: Aspartate aminotransferase, (AST) 40U/L (15-37U/L); alanine amino transferase, (ALT) 40U/L (1 0-40U/L).

Appropriate treatment for brucellosis was initiated. He was discharged from the hospital 5 days after admission on therapy much improved with follow-up appointment.

Discussion

The situation of brucellosis in Saudi Arabia, unlike other countries, is complicated and very difficult to control, the continuous influx of pilgrims during the hajj period and the need for the importation of millions of slaughter animals annually playing a major role.

However, many controllable factors have been implicated in the transmission of Brucellosis and its prevalence in Saudi Arabia, such as the social customs, dietary habits of its people, unregulated importation of poorly screened animals, lack of legislation for proper control of the marketing and movement of animals, husbandry practices, poor animal quarantine procedures and poor cooperation and exchange of information between veterinary and health services. The growing population of Saudi Arabia with its increased demand for dairy products accompanied with changing and intensified farming practices raises the concern for further spread and perpetuation of this disease. Given the complexity of the epidemiology of brucellosis involving various animal species, and multiple risk factors associated, effective control will require a continuous and carefully orchestrated effort by health authorities. An effective national brucellosis control programme is therefore required.

A control programme for human brucellosis would depend to a large extent on good administrative arrangement, ensuring the maximum cooperation of the community, active cooperation between health services and veterinary services and most importantly public health education about the disease and its risk factors.

The eradication of human brucellosis in Saudi Arabia will ultimately depend on the eradication of animal brucellosis. Improved systems for reporting on Brucellosis to the relevant health authorities; health education to high risk groups and the community at large; livestock mass vaccination and improved farm hygiene; implementing legislation to control trade and movement of animals; ensuring the availability of animal quarantine centers; screening and isolation of infected animals can effectively control brucellosis in the animal population and thereby reduce the transmission to the human population.

Mass vaccination of livestock is crucial for the control and eradication of brucellosis together with other measures such as improved farm hygiene,
restriction and control of trade and movement of animals, testing and isolation of infected animals can effectively control brucellosis in the animal population and thereby reduce the transmission to the human population.

Efficient reporting systems for brucellosis cases to health authorities is extremely important as knowledge of the disease prevalence can be used to prioritize a disease control policy for brucellosis and to alert health staff.

In order to reach optimum planning for a national brucellosis control programme in Saudi Arabia, ministerial co-ordination should be established with formulation of inter-governmental veterinary agreements between the Saudi government and the relevant authorities of animal exporting countries.

The epidemiological data on the disease is frequently incomplete. This is partly explained by the lack of proper laboratory facilities in some remote areas as well as by poor cooperation and exchange of information between veterinary and health services.

In spite of the clinical efficacy and cost effectiveness of vaccination, the limited availability of vaccines and lack of awareness has led to the persistence of brucellosis in most areas. High risk groups need to be made aware of the importance of vaccination not only to improve health of their animals but also to reduce the risk of severe illness and disability for themselves and their family members.

The lack of human vaccines and effective control measures make it necessary for health care workers to take protective measures to minimize the risk of infection of the human population. Such measures should include: The control of the disease in animal hosts, improved food hygiene including the pasteurization of milk and proper handling of other animal produce and practice of universal precautions to prevent occupational exposure, such as the use of protective clothing/barriers while handling animals/cultures etc.

Emphasis must be made on the importance of health education of the community. Raising the knowledge and awareness on brucellosis and its causes can greatly help with prevention and control of the disease.

Alertness of medical staff is needed to recognize and diagnose the disease. Brucellosis cases can be easily overlooked and misdiagnosed because of its deceptive nature and the varied clinical manifestations it can present with, making diagnosis quite difficult. Typically patients present with fever of an unknown cause, referred to as pyrexia of unknown origin and symptoms and signs are confused with those of other diseases such as typhoid fever or rheumatic fever. Thus to an unaware physician, the diagnosis of brucellosis can be problematic.

The clinicians should keep in mind the possibility of an occupational or environmental exposure in cases of fever. It would also be worthwhile to create awareness about the disease in such professionals so that necessary precautions and periodic screening of such occupationally exposed people can be done.

The history of travel to endemic countries along with animal contact and food habits could be helpful to raise suspicion of brucellosis and usually critical to making the clinical diagnosis. Laboratory testing is indispensable for diagnosis. Therefore alertness of clinician and close collaboration with microbiologist are essential even in endemic areas to correctly diagnose and treat this protean human infection.

Routine serological surveillance should be practiced in endemic areas. Screening programmes for high risk groups including shepherds, abattoir workers, veterinarians, dairy industry professionals and personnel in microbiologic laboratories should be implemented. Screening of family/household members of index cases of acute brucellosis in an endemic area should be undertaken to pick up additional unnoticed cases. This is an important epidemiological step allowing for timely diagnosis and provision of therapy, which will inevitably result in lower morbidity and mortality rates.
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Brucellosis in Saudi Arabia

54