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Epidemiology and incidence of leishmaniasis in Jazan region, Saudi Arabia (2007-2015): An overview

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Abstract

Cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL) are endemic in Jazan region. Reviewing the epidemiology of leishmaniasis is imperative for the disease surveillance and control. The present study was conducted to investigate the epidemiological trends of leishmaniasis in Jazan region (2007-2015). Secondary data of confirmed cases of CL and VL were analyzed. The total confirmed cases of CL and VL during the said period were 390 and 120, respectively. Aledabi has recorded the highest cases of CL (307), while Alaridah has the highest VL cases (54). Alkhobah recorded the lowest cases for CL and VL (2 and 16, respectively). CL parasite circulating in the region is *Leishmania tropica*, with no animal reservoir host and with *Phlebotomus sergenti* being the main vector. *Leishmania donovani sensu lato* is the main VL parasite in the region; feral dogs are the reservoir, and *P. alexandri* and *P. orientalis* are suspected main vectors. Leishmaniasis is considered an endemic disease in the region. Vector-related interventions would continue to be the intervention of choice.

Keywords: Epidemiology, leishmaniasis, Jazan region, Saudi Arabia

1. Introduction

Leishmaniasis is a group of diseases caused by protozoan parasites from more than 20 *Leishmania* species, and transmitted to humans by the bite of infected female *phlebotomine* sandflies. More than 90 *phlebotomine* sand fly species are known to transmit *Leishmania* parasites. Three main forms of the disease are known as cutaneous, visceral or kala-azar, and mucocutaneous [1]. As much as 0.7–1 million new cases and 20000 to 30000 deaths are reported annually [1]. Leishmaniasis is among the most important six tropical diseases worldwide according to World Health Organization [2].

Leishmaniasis is ranked second in mortality among neglected and tropical diseases and fourth in loss of disability-adjusted life years (DALYs) [3]. It is considered one of the "most neglected diseases" because it occurs mostly in poor countries with limited resources and poor tools for diagnosis, control, and treatment [4, 5].

Cutaneous leishmaniasis (CL) was first described in Saudi Arabia by Moursy and Shoura in 1973. CL is caused by *L. major* in eastern and central regions including Eastern Province, Al-Hasa, Al-Quaseem, Riyadh, and Al-Madinah Al-Monawarah. While *L. tropica* is the main CL causative agent in western and southern regions of the kingdom [6]. Moreover, *L. tropica* was engaged as the causative agent of visceral leishmaniasis in Gulf War veterans. *Phlebotomus papatasi* and *Phlebotomus sergenti* are the main vectors of CL in the Kingdom, while *Meriones libycus* and *Psammomys obesus* (Sand rat) are the principal reservoir hosts for the CL in Al-Qaseem, Al-Hassa, and Al-Madinah [6].

Over 90% of the global cases of visceral leishmaniasis (VL) are reported from six countries: Brazil, Bangladesh, India, Ethiopia, South Sudan, and Sudan [7]. Whereas two-thirds of CL cases are reported from six countries: Algeria, Afghanistan, Brazil, Colombia, Syria, and Iran [8].

Incidences of the visceral leishmaniasis (VL) in Saudi Arabia are sporadic and restricted to the southwest region (Asir and Jazan) [1]. *Leishmania donovani sensu lato* causes the VL in Jazan region [9].

The total CL cases in Saudi Arabia throughout the period from 2007 to 2015 were 21368, while for VL the total was 138 cases [10]. The most endemic regions by the CL with constant endemicity are Al-Hassa, Madinah, Ha'il, and Al-Qaseem [6].

Sand fly fauna surveys in Saudi Arabia revealed the presence of 25 species all over the Kingdom with the predominance of *Phlebotomus papatasi* [11, 12, 13]. Studies showed that ten species distributed within two sand fly genera have been identified in Jazan region. These are; *Phlebotomus papatasi*, *P. bergeroti*, *P. sergenti*, *P. savevus*, *Sergentomyia antennata*, *S. africana*, *S. schwetzi*, *S. tiberiadis*, *S. fallax* and *S. magna* [14]. Despite the endemic state of leishmaniasis in Jazan region, the disease is rarely studied. Therefore, we conducted the present study to review the epidemiology and incidence status of both CL and VL in the region during the period of 2007-2015. We

also report the endemic parasites, vectors, and reservoirs of leishmaniasis in the region, their diagnostic methods, treatment, risk factors, and future perspectives.

2. Study area

Jazan region (Fig.1) is situated in the subtropical zone, Southwest Saudi Arabia, lies between 16°-12, and 18°-25, latitude north. It is surrounded by the Red Sea (260 km) from the west and by Arabic Republic of Yemen (120km) from the south and east, and Asir region from the north, with total area of about 22,000 km2 and 1,365,110 populations (the 2010 census).

The region is divided into 10 governorates; Al-Raith, Baish, Damad, Farasan, Ahad-al-Masarha, Al-Harth, Alaridah, Al-Qeiyas, Aledabi and Al-Dai'yer [15].



Fig 1: The Map of Jazan Region Showing its Different Governorates

3. Epidemiology of Leishmaniasis in Jazan region

3.1 Epidemiology of CL in Jazan region

The total cases reported during the period from 2007 to 2015 were 390 (equal to 1.8% of the total cases of CL in the kingdom for the same period). The highest number of cases were recorded in 2010 (82) and the lowest were in 2015 (8) (Fig.2).

The distribution pattern of CL cases in Jazan region (2007-2015) according to gender showed that 64% of the total cases were males (250), whereas 36% were females (140). This may be attributed to the fact that males are more exposed to the sand fly bites than females in Saudi Arabia [16]. Moreover, women are traditionally protected from sand flies' bites because the most parts of their bodies are covered by the Islamic dress. Notably, 98.7% of the cases were Saudi and the rest were non-Saudi (1.3%). Moreover, the high incidence of CL in the region was in the 15 years and above age group (38.9%) followed by the 10-14 years' age group (22.5%), the 5-9 years' age group (18.5%), the 1-4 years' age group (17.8%) and the lowest was in the < 1-year age group (2.3%) (Table 1).

On the other hand, the spatial distribution of the CL cases revealed that Aledabi had recorded the highest number (307), followed by Haroub (70), Alaridah (11), and Alkhobah (2) (Table 2).

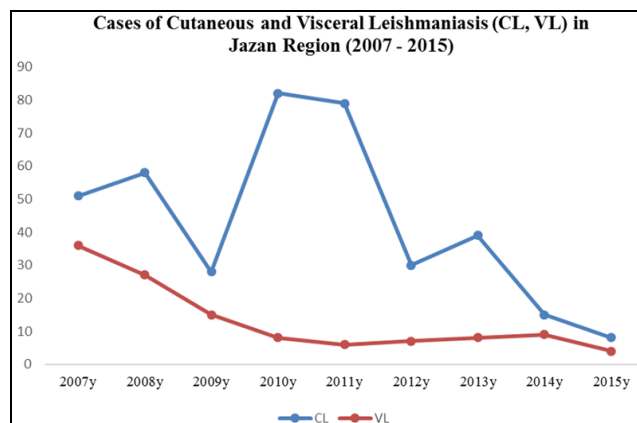


Fig 2: Cutaneous and Visceral Leishmaniasis (CL, VL) Cases in Jazan Region (2007 - 2015)

As far as the characteristics of cutaneous leishmaniasis in Jazan region is concerned, results of randomly selected patients (177) show that 122 patients had lesions on their faces, while 44 had the lesions on their hands, 7 on legs, and 4 on other places of their bodies (Table 3). Likewise, 45 of the CL patients had 2 scars, 1 patient with 3 scars, and 3patients with more than 3 scars (Table 3).

3.1.1 Endemic CL Parasites in the region

Leishmania parasite circulating in Jazan region and responsible for CL is *L. tro //kl. ; p ;/ pica* in both highlands (2000 m altitude) and lowlands (450-700 m altitude)^[9].

Parasite isolates from the lowlands showed that only one

zymodeme (LON-63) was found, whereas four zymodemes (LON-10, 71, 72 and 73) were found in highland^[9]. In other regions of the Kingdom i.e. Al-Qaseem, Al-Madinah, Ta'if and Al-Bahah, both *L. tropica* and *L. major* were found to be the causative agents for CL in the same region^[17, 18, 19, 20].

Table 1: Distribution of CL Cases in Jazan Region According to Gender, Nationality and Age Groups (2007-2015)

| Year | Number of cases | | Nationality | | Age groups | | | | |
|---------|-----------------|---------|-------------|-----------|------------|-----------|-----------|-------------|--------------------|
| | Males | Females | Saudi | Non Saudi | < 1 year | 1-4 years | 5-9 years | 10-14 years | 15 years and above |
| 2007 | 34 | 17 | 51 | 0 | 0 | 7 | 12 | 7 | 25 |
| 2008 | 43 | 15 | 58 | 0 | 2 | 11 | 12 | 12 | 21 |
| 2009 | 16 | 12 | 28 | 0 | 2 | 5 | 4 | 6 | 11 |
| 2010 | 48 | 34 | 82 | 0 | 3 | 19 | 14 | 20 | 26 |
| 2011 | 50 | 29 | 77 | 2 | 0 | 13 | 12 | 26 | 28 |
| 2012 | 15 | 15 | 30 | 0 | 0 | 6 | 5 | 6 | 13 |
| 2013 | 26 | 13 | 36 | 3 | 0 | 5 | 10 | 9 | 15 |
| 2014 | 13 | 2 | 15 | 0 | 2 | 3 | 3 | 2 | 5 |
| 2015 | 5 | 3 | 8 | 0 | 0 | 0 | 0 | 0 | 8 |
| Total | 250 | 140 | 385 | 5 | 9 | 69 | 72 | 88 | 152 |
| Percent | 64% | 36% | 98.7% | 1.3% | 2.3% | 17.8% | 18.5% | 22.5% | 38.9% |

Table 2: Spatial distribution of CL cases in Jazan region (2007-2015)

| Governorate | Year | | | | | | | | | | Total | Percent |
|-------------|------|------|------|------|------|------|------|------|------|-----|-------|---------|
| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | | | |
| Aledabi | 39 | 52 | 20 | 53 | 68 | 29 | 32 | 11 | 3 | 307 | 78.7% | |
| Haroub | 10 | 4 | 8 | 29 | 8 | 1 | 4 | 4 | 2 | 70 | 17.9% | |
| Alaridah | 0 | 2 | 0 | 0 | 3 | 0 | 3 | 0 | 3 | 11 | 2.8% | |
| Alkhouba | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0.6% | |
| Total | 51 | 58 | 28 | 82 | 79 | 30 | 39 | 15 | 8 | 390 | 100% | |

Table 3: Characteristics of Cutaneous Leishmaniasis (CL) in Jazan region, Saudi Arabia (N=177)

| Characteristics | Frequency | Percent |
|------------------------|-----------|---------|
| Lesions | | |
| On face | 122 | 68.9% |
| On hand | 44 | 24.9% |
| On leg | 7 | 3.9% |
| Others | 4 | 2.3% |
| Number of scars | | |
| 2 scars | 45 | 92% |
| 3 scars | 1 | 2% |
| More | 3 | 6% |

3.1.2 Endemic CL Vectors in the region

The major vector of *L. tropica* in the highlands is *Phlebotomus sergenti* and proved to be the dominant species in all areas. Entomological researches indicated the existence of six species of *Phlebotomus* in the southwest region of the Saudi Arabia including Jazan with *Ph. sergenti* as the dominant species in the highlands and *Ph. bergeroti* in the lowlands. Other species including *Ph. arabicus* which is limited to high altitudes, *Ph. alexandri* confides to low altitudes, and *Ph. orientalis* mainly found in the highlands. The seasonal distribution of those vectors revealed that July is their population peak^[9]. This finding is similar to other work done in northwestern of Saudi Arabia in which *Phlebotomus papatasi* and *Sergentomyia clydei* were found to be active from April to November with their peak activities being in July through August^[21].

3.1.3 CL Reservoirs in the region

It is stated that man is considered the main reservoir for *L. tropica*^[22]. However, dogs in Russia have been found infected in endemic areas^[23].

3.2 Epidemiology of VL in Jazan region

The ecology and epidemiology of visceral leishmaniasis (VL) in Jazan region are determined by characteristics of the sand fly species, parasite species, and reservoir hosts (mammalian reservoirs). However, four types of foci of VL had been described as follows^[23]; i. Natural foci: the transmission occurs from animal to animal through the sand fly vector. Man is involved accidentally. ii. Semi-synanthropic: Where transmission occurs between wild animals and domestic animals and man through the vector. iii. Synanthropic: Where the dog is the main reservoir of infection and man is frequently involved. iv. Endemic foci of Indian kala-azar: Where only man is involved.

VL is endemic in Jazan region and occurs eventually in the region in numbers more than any other regions of the Saudi Arabia. The total VL cases throughout the period from 2007 to 2015 were 120 (equal to 87% of the total cases of VL in the kingdom for the same period) (Table 4). The highest number of cases were recorded in 2007 (36) and the lowest were in 2015(4) (Fig.2).

The distribution of VL cases in Jazan region (2007-2015) according to gender showed that 58.3% of the total cases were males (70), while 41.7% were females (50). In addition, 75.8% of the cases were Saudi and the rest were non-Saudi (24.2%). Moreover, the high incidence of VL in the region was in the 1-4 years old age group (53.3%) followed by the 5-9 years' age group (24.2%), the < 1-year age group (16.7%) and the lowest was in the 10-14 years' age group (5.8%) (Table 4). Similar results were attained in Jazan region where high incidence of VL was observed in the 1-4 years old age group and the lowest was in the 10-14 years old age group^[24]. Likewise, the maximum cases of VL in Italy were in the age group from 1-3 years^[25].

Table 4: Distribution of VL Cases in Jazan Region According to Gender, Nationality and Age Groups (2007-2015)

| Year | Number of cases | | Nationality | | Age groups | | | |
|---------|-----------------|---------|-------------|-----------|------------|-----------|-----------|-------------|
| | Males | Females | Saudi | Non Saudi | < 1 year | 1-4 years | 5-9 years | 10-14 years |
| 2007 | 19 | 17 | 34 | 2 | 7 | 20 | 7 | 2 |
| 2008 | 16 | 11 | 21 | 6 | 3 | 13 | 9 | 2 |
| 2009 | 9 | 6 | 12 | 3 | 1 | 6 | 7 | 1 |
| 2010 | 3 | 5 | 4 | 4 | 2 | 4 | 1 | 1 |
| 2011 | 3 | 3 | 6 | 0 | 1 | 4 | 1 | 0 |
| 2012 | 6 | 1 | 5 | 2 | 2 | 5 | 0 | 0 |
| 2013 | 4 | 4 | 2 | 6 | 1 | 4 | 2 | 1 |
| 2014 | 8 | 1 | 4 | 5 | 1 | 6 | 2 | 0 |
| 2015 | 2 | 2 | 3 | 1 | 2 | 2 | 0 | 0 |
| Total | 70 | 50 | 91 | 29 | 20 | 64 | 29 | 7 |
| Percent | 58.3% | 41.7% | 75.8% | 24.2% | 16.7% | 53.3% | 24.2% | 5.8% |

As for the spatial distribution of the VL cases, Alaridah has recorded the highest number (54), followed by Aledabi (28), Haroub (22), and Alkhobah (16) (Table 5). It is stated that most of the cases are originated in the lowlands of the region from rural and semi-rural areas which characterized by clay soils and hot climate [9].

3.2.1 Endemic VL Parasites in the region

The nature of the parasite has been confirmed by Isoenzyme typing as *Leishmania donovani* sensu lato zymodeme LON-42 [26]. The parasite is identical to the zymodeme of *L. donovani* of east Ethiopia and different from zymodeme of *L. donovani* from India and from typical *L. infantum* of Tunisia. It causes zoonotic infantile kalaazar in the lowland areas of Jazan [9].

3.2.2 Endemic VL Vectors in the region

Both *P. alexandri* and *P. orientalis* are suspected as the main vectors of *L. donovani* sensu lato zymodeme LON-42 in Jazan region [27]. In east Africa, *P. orientalis* is the main vector of VL in Sudan [28] and Ethiopia [29]. While *P. alexandri* is the main vector of VL in the area from North Africa to western China [30].

3.2.3 VL Reservoirs in the region

Zoonotic Infantile Kala-azar is caused by *L. tropica* and *L. donovani* sensu lato zymodeme LON-42 in areas at altitudes of up to 700m [9].

Feral dogs were found to be the animal reservoir for *L. infantum* in the region. A high prevalence rate of *L. infantum* in dogs (19.3%) was reported [9].

Table 5: Spatial Distribution of VL Cases in Jazan Region (2007-2015)

| Governorate | Year | | | | | | | | | Total | Percent |
|-------------|------|------|------|------|------|------|------|------|------|-------|---------|
| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | | |
| Alaridah | 19 | 10 | 5 | 3 | 2 | 2 | 8 | 4 | 1 | 54 | 45% |
| Aledabi | 7 | 4 | 5 | 3 | 2 | 3 | 0 | 2 | 2 | 28 | 23.3% |
| Haroub | 3 | 8 | 3 | 1 | 2 | 1 | 0 | 3 | 1 | 22 | 18.3% |
| Alkhoubah | 7 | 5 | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 16 | 13.4% |
| Total | 36 | 27 | 15 | 8 | 6 | 7 | 8 | 9 | 4 | 120 | 100% |

3.3 Major risk factors

The major risk factors for leishmaniasis include population mobility, urbanization, malnutrition, drought, floods, fluctuations in climatic factors especially temperature, rain fall, and humidity can affect both vectors and reservoir hosts [1].

It is worthy to highlight that factors increase the likelihood of progressing from CL infection to clinical VL include age <5 years (for *L. infantum* infection), host immunogenetic factors, poor nutritional status, and HIV co-infection [31, 32, 33].

3.4 Clinical Features

Common clinical features of CL include a raised papule lesion which turns later to a nodule or a plaque after many weeks, with crust formation and ulceration located at the center of the lesion. On other hand, satellite lesions are known

to occur with *L. major* infections. The commonly affected sites of exposed parts of the body are the face, neck, arms, and legs [6] (Fig.3 A1, A2). Scars could be 2 or 3 or more (Table 3).

General and common clinical features of VL in Jazan are prolonged fever, progressive abdominal distention, general weakness, weight loss, recurrent infections, (most patients are from mountainous zone and their age usually 4months to 5 years) (personal communication with the pediatric infectious diseases unit, King Fahad Central Hospital, Jazan) (Fig.3 B).

Other authors also reported the predominant clinical features of VL in Jazan region to include chronic fever, hepatosplenomegaly, weight loss, and abdominal distention. While, laboratory abnormalities included hypoalbuminemia and hypergammaglobulinemia, leucopenia, anemia, and thrombocytopenia [34].



Fig 3: A1, A2: Patients Presenting Lesions of Cutaneous Leishmaniasis. B: A Child with Visceral Leishmaniasis Showing Hepatosplenomegaly.

3.5 Diagnosis

Microscopic examination of Giemsa stained lesion biopsy smears (CL); or bone marrow (VL) are the most currently applied approaches for identification of leishmanial organisms in Jazan region.

3.5.1 CL Diagnosis

Aside from the clinical diagnosis, microscopic smears from scraping or skin biopsy are used for CL diagnosis to identify amastigotes of leishmania in the specimen (Giemsa stained lesion biopsy smears). Aspirate and biopsy materials from the edge of lesions can also be cultured in NNN or Schneider medium to detect the diagnostic stages (promastigote) of the parasite [16].

3.5.2 VL Diagnosis

The commonly used and applied method to detect the diagnostic stages (amastigotes) of visceral leishmaniasis in Jazan region is based on the microscopic examination of Giemsa stained bone marrow aspirates (BMA) [35, 7].

It is worthy to note that the direct microscopic examination in both cases (CL and VL) is rapid and low-cost effective, but with very low sensitivity especially when parasites are low abundant such as in case of chronic infection [35].

3.6 Treatment

3.6.1 CL Treatment

Although CL is thought to be a self-healing disease, drugs are used to treat CL in order to minimize the resultant scars from the lesions.

The Pentavalent antimony compound; Sodium stibogluconate (pentostam) is the most widely used drug to control the CL in Jazan region.

In addition to pentostam, cryosurgery using liquid nitrogen as the cryogen is also used in certain cases. Three to four cycles of 10-30 s freezing time were used and repeated at weekly intervals (personal communication with Dr. Adel Arishi of Prince Mohamed Bin Nasser Hospital in Jazan).

3.6.2 VL Treatment

Depends on bone marrow aspirate (BMA) results, there are two options to treat VL in Jazan region:

- Liposomal amphotericin- is considered the first line choice. Dose: 3mg /kg/day intravenous (IV) infusion over 2-3 hours for total of 7 doses. The last two doses will be on day 14th and 21st of therapy. The FDA approved dose regimen [36].
- Sodium stibogluconate (pentostam). Dose: 20mg /kg /day x 28 days Drug is given intravenous (IV) during admission and

continued intramuscular (IM) after discharge. This drug is used if Liposomal amphotericin is not available or if there is a contraindication (personal communication with Dr. Hayder Arishi of King Fahad Hospital in Jazan).

4. Future Perspectives

Polymerase Chain Reaction (PCR) showed high sensitivity and specificity in confirming clinically suspected cases of leishmaniasis. It should be used in detection of the leishmanial parasites in laboratories in Jazan region.

Development of an efficient vaccine against leishmanial parasites is badly needed.

Future efforts required in Jazan region to combat leishmaniasis include suitable disease surveillance system, sustainable source of treatment, continuation of the existing vector control program, and raising the public awareness of the disease and its complications especially among children under 14 years (VL) and adults (CL).

5. Conclusion

To conclude, both CL and VL are considered endemic diseases in Jazan region although with declining incidences. More efforts on the control of parasites and vectors are required, augmented by animal host reservoirs culling. Vector-related interventions would continue to be the intervention of choice especially in the most affected Governates; Aledabi, Alaridah, Haroub, and Alkhobah. Health education on the use of personal protection measures should be performed regularly throughout the region to prevent many vector borne diseases, including CL and VL. Studies to reassess the epidemiology of leishmaniasis in the region are badly needed to determine the disease burden. This should include identification of the involved parasite, regular evaluation and assessment of sand flies' density, behavior and distribution.

Development of regional diagnostic and management guidelines are extremely needed.

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