

A clinicoepidemiological study on kala-zar disease from areas infested with the *Leishmania donovani* in Al-Muthanna province, Iraq

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Abstract:

Kala azar is a predominant parasitic disease with different clinical manifestations in Al-Muthanna. It represents an important public health problem because of its impact on many individuals, its spread and deaths, as well as the difficulties in applying effective control measures. Therefore, this current study was conducted to describe the demographic and epidemiological features of kala azar disease in the province. A descriptive study was applied to twenty five patients selected from the province, six in Al-Rumaitha Hospital, ten in the Children's Hospital in Al-Samawa, five cases in Al-Khidr Hospital, in addition to four cases in Al- Warka, and these cases were distributed as four in 2016, three in 2017, three in 2018, eight patients in 2019, four patients in 2020 and three patients in 2021. Collect and analyze data such as gender, age, season of infection, time of illness, method of diagnosis, patient outcome, clinical symptoms and place of residence through descriptive statistics. The highest percentage of kala azar was in females by (60 %), and the study showed that the highest percentage of visceral leishmaniasis cases was in January and February, and it began to decline gradually, reaching its lowest rate in August. It was also found that the highest incidence of visceral kala azar was in the age group 1-4 years, while the lowest rate was in the older age group. The geographical distribution of kalazar showed a high percentage of infection in Al-samawa city, with regard to the difference between urban and rural areas, the data revealed the highest recording of cases in rural areas, while the rates were lowest in urban areas. For patients who received health care, the cases of recovery from kalazar were higher by (80%), and it was also noted that the highest percentage of clinical symptoms associated with infection in all patients are spleen enlargement and anemia, followed by enlargement of the liver and lymph nodes in lower rates.

Kala azar is likely to affect the rural areas of Al-Muthanna. According to the epidemiological features of visceral leishmaniasis in the county, this disease remains a health hazard and must be managed, under a unified mechanism of control and prevention. Thus, measures such as staff training, screening in endemic areas, and more efforts in rural areas can be beneficial.

Keywords: *Kala azar*, *Leishmania donovani*, visceral leishmaniasis.

Introduction

Leishmania donovani produces visceral leishmaniasis (Kala Azar): Symptoms include fever (two bouts of fever per day) likely to reach 40-41°C, dilation of the spleen and liver, weakness, and persistent wasting. The disease is often fatal without treatment, but survivors often develop immunity. Signs and symptoms include: low red and white blood cell counts, fever, enlarged spleen and liver, splenomegaly, hepatomegaly, diarrhea, bleeding, ascites, and weight loss. In this case, the internal organs are affected. Anemia, responsible for the severe pallor of the skin and mucous membranes, which gives a gray appearance to patients, for that (kala azar - black fever) and this is the most dangerous form of the disease, as it is fatal without treatment [1]. Species of the *L. donovani* complex (*L. donovani*, *L. infantum* and *L. chagasi*) are the principal causative agents of visceral leishmaniasis, also known as kala-azar or Dum-Dum fever. Also, *leishmania tropica*, in the Old World and *leishmania amazonensis* in the New World. Usually, VL has an incubation period that varies from 2 to 4 months leading to several clinical presentations asymptomatic, acute and chronic [2].

Visceral leishmaniasis and cutaneous leishmaniasis caused by *Leishmania donovani* and *Leishmania tropica* or *Leishmania major* respectively are known endemic diseases in Iraq. Visceral leishmaniasis had been prevalent in Iraq for the last 2-3 decades causing serious problems. It represents an important factor in infant's mortality in this country [3].

Leishmaniasis is a disease caused by a group of animal organisms of the genus *Leishmania*, as well as from (500) species of insects belonging to the known species of *Phlebotomus*, of which (30) were positively identified as vectors of the disease, where the female sand fly transmits the primary organisms and the geographical distribution of the disease depends on the distribution of sandflies and the area exposed to the cold climate. Visceral leishmaniasis has been the cause of severe suffering and death for hundreds of years [4].

Visceral leishmaniasis (VL) is one of the most important endemic diseases in Iraq and is known to occur since (1916) when first infection with *Leishmania* was recorded. In Iraq, the disease was found to be more prevalent in the central region (Al- Najaf, Babil, Karbala, and Al-Qadisiyyah provinces) and mostly in the rural village, area and semi-desert region [5,6]. In southern Iraq the main focus of visceral leishmaniasis was in the province (Maysan, DhiQar, Basra and Muthanna) [7].

There are fifteen species of sandfly in Iraq, but the paptassi species is responsible for the transmission of the disease to humans [8]. Leishmaniasis is transmitted from one person to another through the bite of an infected insect, a female sandfly of the genus *Phelebotomus*. Members of the canine family and rodents may play the role of the storage host in the life cycle. The parasite exists in two different stages during its life cycle. Amastigote, which is found inside the cells of the reticuloendothelial system of the vertebral host, and the promastigote, which is found in the intestines of the vector.

Visceral Leishmaniasis, also known as Blak Fever or Kala-azar, is the most dangerous, as the parasite invades the internal organs, including the liver, the spleen, and the bone marrow [9].

An early diagnosis of Leishmaniasis is crucial as the disease is a serious infection for both communities and individuals. To date, no single approach has been accepted as the gold standard means of diagnosing Leishmaniasis. However, there are two general ways of diagnosing the disease which are clinical signs and laboratory tests. In kala azar disease, many signs can be used as infection indicators such as irregular fever, weight loss, spleen inflation, abdominal pain, loss of appetite, cough, joint pain, skin darkness, bleeding (especially nosebleeds) and emaciation. However, even though kala azar disease has their early symptoms, the clinical signs might lead to misdiagnosis as kala azar disease symptoms might be confused with other similar conditions such as Malaria, Schistosomiasis, Leukemia, Tropical Splenomegaly and Millitary Tuberculosis. Hence, there are some reservations about clinical diagnoses and a laboratory test is believed to be the best option in the case of any suspicion of Leishmaniasis infection to get a definite answer. These laboratory methods include parasitological, immunological and molecular tests [10].

The aim of the research

The occurrence of this disease in Iraq and in a large proportion in different regions of the country, especially the province of Al-Muthanna, drew the attention of researchers to focus on studying the disease in a large way, relying on the available statistics, and educating citizens about the serious damage it causes. Illness affects public health, especially children.

The aim of the present study is to describe and summarize data from all registered cases of VL in Al-Muthanna province from 2016-2021, by demographic information and geographic distribution and to compare the results with those published for other areas in Iraq and endemic countries, as well as clarifying some of the epidemiological characteristics and the source that causes visceral leishmaniasis in Al-Muthanna province. Also, to know the differences about the distribution of the disease among all districts of Al-Muthanna province

Methodology

Study area

Al-Muthanna Governorate is located in southwestern Iraq, and shares internal borders with the governorates of Najaf, Qadisiyah, Dhi Qar and Basra. The climate in Muthanna is a dry desert climate. In summer temperatures easily exceed 40°C, while rainfall is very limited and limited to the winter months. The population is concentrated along the Euphrates River in the north of the governorate, while the southern desert areas are sparsely populated. The governorate is divided into five regions: Samawa, Al-Khader, Al-Rumaitha, Al-Warka and Al-Salman.

The study periods

The current study aimed to determine the epidemiological aspect of visceral leishmaniasis in Muthanna province during (six years) the year 2016-2021.

The Importance of research

The aim from research is the result that we seek to reach, and then we formulate those results in a way that sheds light on the goals related to the phenomenon of the most dangerous and deadly diseases in Iraq in general and Al-Muthanna Governorate in particular. The most important objectives of the study can be identified as follows: (1) Knowing the increase in the incidence of kala azar disease in the governorate. (2) Follow the chronological development of kala-azar infection. (3) Determine the immediate and future consequences of the injury.

Sources of data and information

The study relied on the data provided by the records of patients with communicable diseases in the centers for communicable disease control and patient files in hospitals and provincial centers. In addition to the zoonotic disease control plan issued by the Department of Health Planning. Ministry of Health and Environment / Public Health Department. This study was conducted on 25 patients with Kala azar, who were treated in four districts of Al-Muthanna Governorate. The study used the disease surveillance database available from the Department of Epidemiology and Communicable Disease Control.

Results and discussion

Monitoring and Early Diagnosis of Visceral Leishmaniasis:

Standard definition of disease:

Possible case: a person who lives in or has traveled to endemic areas with visceral leishmaniasis and who shows clinical signs and symptoms of visceral leishmaniasis (persistent irregular fever for more than 2 weeks, splenomegaly, with/or weight loss).

Confirmed case:

Laboratory Confirmed Case: A probable case with laboratory confirmation, either serological (RDT, IFAT) and/or parasitological (swab, culture) and/or positive by PCR or related techniques.

Clinically Confirmed Case: A potential case that has not been confirmed by any laboratory test but has been evaluated by a physician based on clinical grounds.

Initial assessment (at the end of treatment)

Initial recovery: The course of treatment was completed and the patient clinically improved. That is, "no fever + regression of spleen enlargement (even if partially) + return of appetite with/or increase in body weight".

Failure (non-response): Signs and symptoms persist or return during treatment or until the results of initial treatment have been evaluated.

Loss to follow-up/unknown: the patient did not show up for the initial assessment after completing treatment, or the patient's condition was not recorded.

Death: death of anyone diagnosed with visceral leishmaniasis, regardless of treatment status and cause of death, in the standard post-treatment follow-up period.

Final evaluation (6 months after the last medication .)

Final cure: A patient who, after gaining initial recovery, remains symptom-free six months after completing treatment.

Relapse: A patient presents with a recurrence of symptoms of visceral leishmaniasis with parasitological confirmation at any time after the acquisition of an initial cure.

Death: death of any person diagnosed with visceral leishmaniasis, regardless of treatment status and cause of death, in the standard post-treatment follow-up period.

Loss of follow-up: the patient did not show up for evaluation at six months.

Number of cases in Iraq during study years

Visceral leishmaniasis (VL) is a parasitic disease found mainly in tropical and subtropical regions. It is a chronic systemic disease that mainly affects children under the age of five; It may be associated with malnutrition and other conditions of immunosuppression such as HIV/AIDS. If adequate treatment is not started in time, it can progress to death in 90% of cases. The following is a Table 1 showing the numbers of injuries and deaths during the 2016-2020:

Table 1. Numbers of injuries and deaths in Iraq from 2016-2020

Year	Numberof infections	Injury rate per 100,000 population	Deaths	Death rate % of infections
2016	183	0.48	1	0.5
2017	172	0.46	2	1.16
2018	259	0.67	2	1.15
2019	381	1.06	19	5
2020	437	1.18	14	3.2

The following figure 1 shows the number of injuries in Iraq during the five years from 2016-2020, and we noticed a clear increase in injuries since 2017.

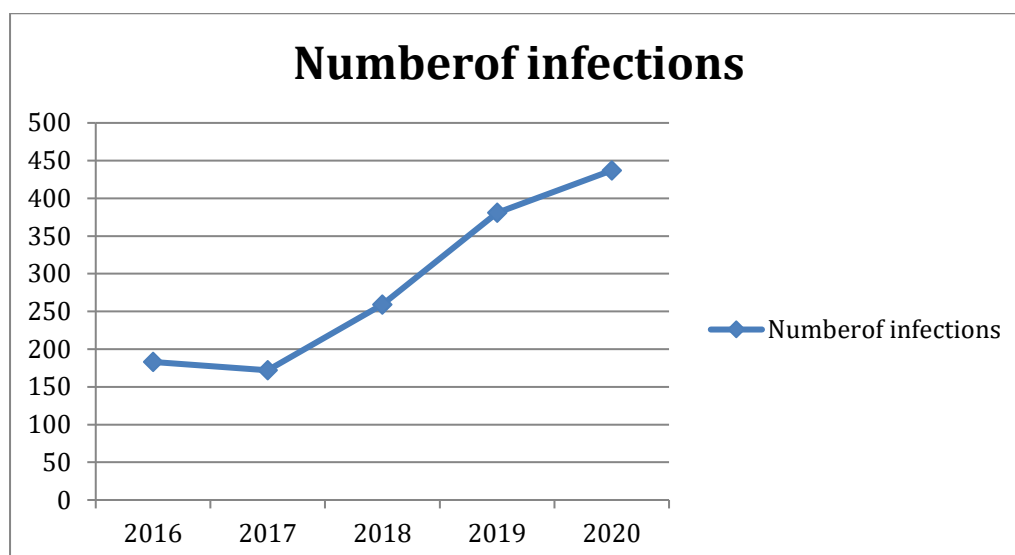


Figure 1. Numbers of infections in Iraq from 2016-2020.

Number of cases in Al-muthanna province during study years

The following figure 2 shows the number of injuries in Al-Muthanna Governorate during the study years from 2016-2021, and we noticed a clear increase in injuries in the year 2019, then it began to decrease, unlike what is found throughout Iraq.

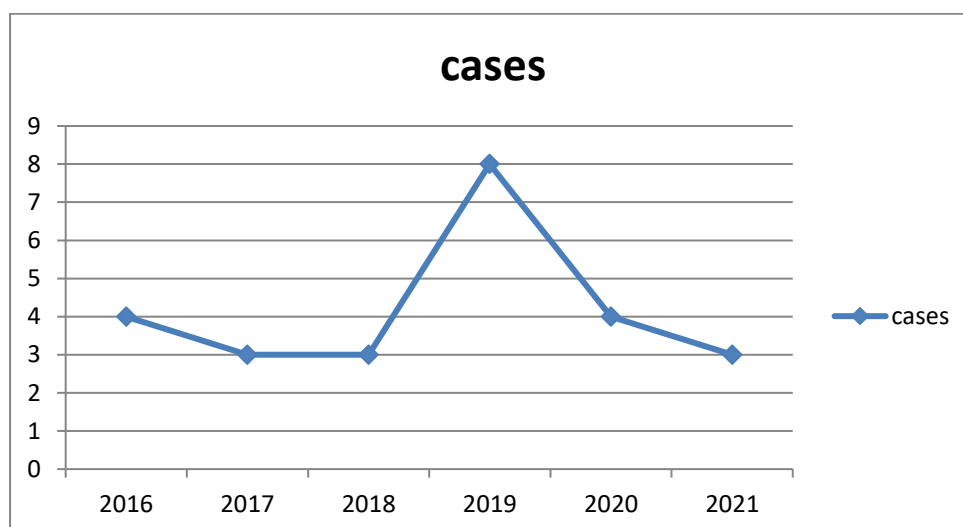


Figure 2. Number of cases in Al-muthanna province during study years.

Distribution of cases according gender

The results showed as in Fig. 3 that the cases of Kala azar were higher in females by (60 %) than the total cases, while it was 40 % in males. These results are similar to previous studies in Iraq and some other countries [11], and to justify this result, women in rural areas are more likely to contract the disease, where they have to take care of livestock and poultry, and there are a lot of flies inside animal pens. While other studies indicate that the infection rate of males is higher than females, the reason

is that males are more exposed to sand flies than females, especially those recorded in central and southern cities Iraq [12]. Despite differences in male to female ratios, males account for more kala azar cases in all regions. These observations can result from parasitic, host, or societal factors, or a combination of these variables [13]. An example is visceral leishmaniasis caused by *L. donovani* in the Indian subcontinent and other regions of the world, where biological and gender factors can contribute to setting differences in disease severity between the sexes [14].

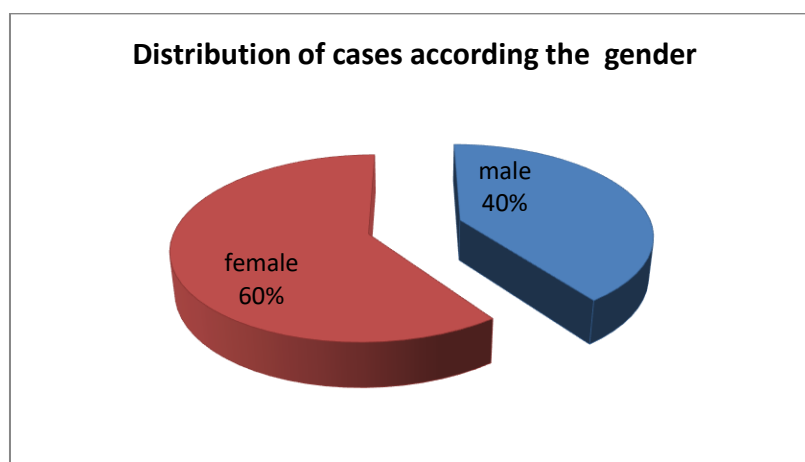


Figure 3. The distribution of cases by gender.

Geographical distribution

Figure 4 shows the geographical distribution of visceral leishmaniasis infections. The Data revealed the highest percentage in Al- Samawah (40%), while the lowest cases were recorded in Rumaitha (24%) and khidir (20%) and Warka (16%). The results of the study were supported by previous studies that reported that five Iraqi governorates are hotbeds of leishmaniasis in Mosul. Baghdad, Karbala, Muthanna and Maysan [15], and the geographical distribution showed that the disease is more prevalent in Iraq. The southern and central region of Iraq, and spread in the northern and central parts of Iraq. The majority of cases were diagnosed from rural areas with high soil moisture due to the presence of numerous interconnected rivers and canals, as well as dense vegetation. These factors may provide a suitable environment for sand flies to breed [16]. Parasitic diseases in Iraq, including leishmaniasis, represent a serious public health problem. Several factors play important roles in the presence and distribution of these diseases in different regions of Iraq, including the use of mud to build many houses in villages. Furthermore, people who work long hours outdoors are more susceptible to sand bites [17].

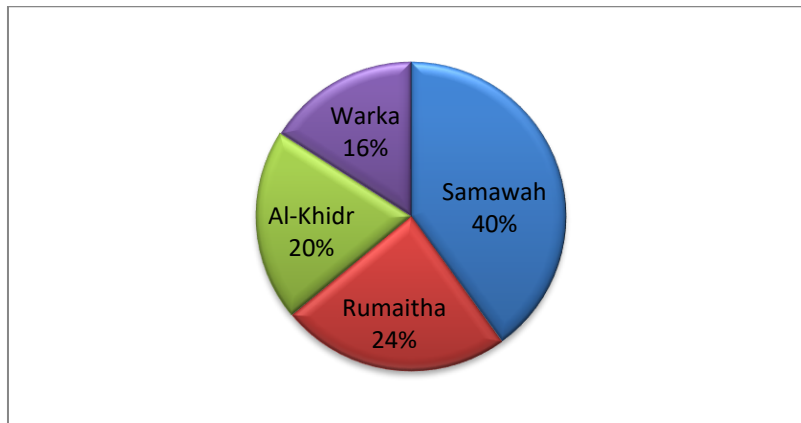


Figure 4. The geographical distribution of cases

With regard to the difference between urban and rural areas, the highest cases were recorded in rural areas (63%), while the lowest were recorded in urban areas (37%). This large difference Figure 5 is consistent with the results reported in Iraq where Al-Obaidi (2016) stated that cutaneous leishmaniasis is more common in rural areas than in urban areas [18]. Most recent studies show that poorer farmers in rural areas may live close to their animals, which enhances moisture and organic matter synthesis for breeding sand flies [19].

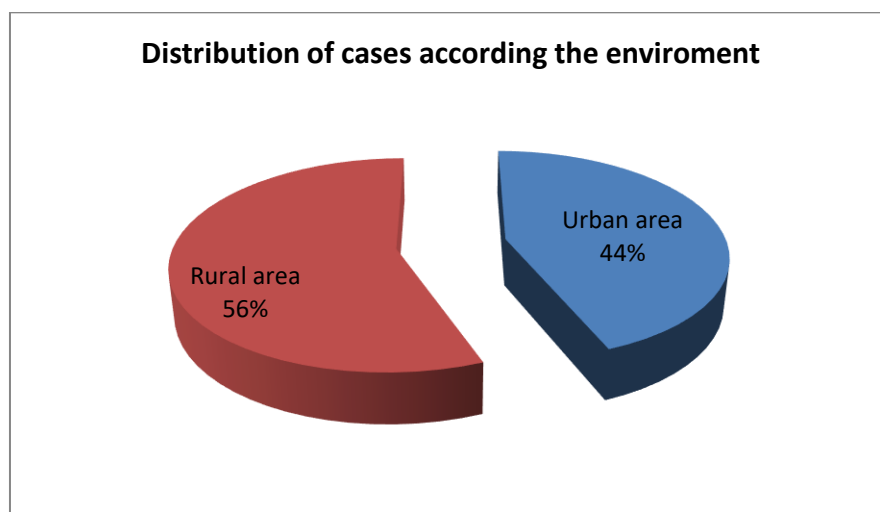


Figure 5. The distribution of cases according to the environment.

There are many factors that play an important role in the presence and spread of new leishmaniasis in rural areas, including the presence of animals that constitute a reservoir for this disease, especially rodents and dogs, and also the presence of swamps that provide the appropriate environment, which helps the insect to grow during its life cycle. In the larval stage of the worm, the insect needs to fertilize the soil and animal feces to feed it, which is provided by the soil surrounding the swamps, as well as there are some houses built of mud, especially those in villages. Rural areas,

especially agricultural ones, are attractive and harbor many types of insects, so people will be more susceptible to sand fly bites.

Monthly distribution of cases

The study shows that the lowest infection rate was in August 2019 as well as all years, and then began to rise to reach the highest infection rate in January 2019 and February 2020 (Figure 6). (Jalil Abu Al-Hab) stated that cutaneous leishmaniasis occurs in September [20]. When comparing the cases in this study, we find that the expected infections occur during the month of September and appear in the month of January after an incubation period of four months, which is the incubation period of the main species (the rural type).

These results appear in Figure 5 similar to the results of [21], where the summer and hot months of the year are the most common infections in accordance with the activity of the insect and its density, where the incubation period varies because of the immune response of the host and the difference in the species so that symptoms start to appear at the end of the Autumn and the beginning of winter.

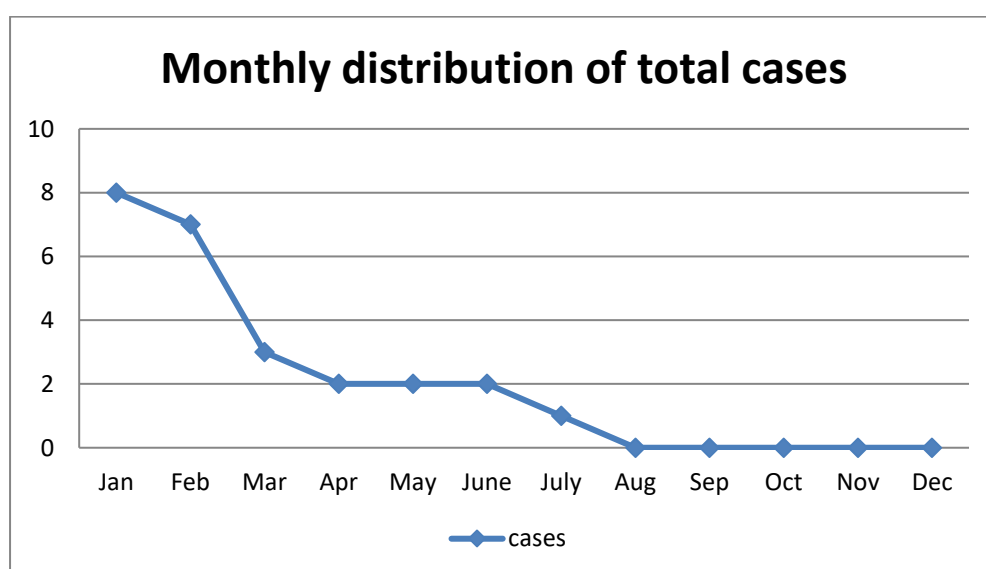


Figure 6. The monthly distribution of total cases.

Distribution of injuries according to age groups

The highest incidence of visceral leishmaniasis was observed in the age group (1-4 years), reaching (58%). The disease was found to affect all age groups (Figure 7). The results are close to the study [22], which indicated that leishmaniasis is common in children under 12 years of age in affected areas. The results were similar to the study [23], which reported that the number of victims decreased according to the age group. Most cases are found in young age groups, because the immune system is not fully developed, and children are more susceptible to insect bites, especially during sleep [24].

The incidence of leishmaniasis is significantly higher among children than in other age groups, and the reason may be the child's lack of awareness during an insect bite and the weakness of the immune system in children, as well as the difference in behavior and movement during sleep in children compared to the percentage of adults.

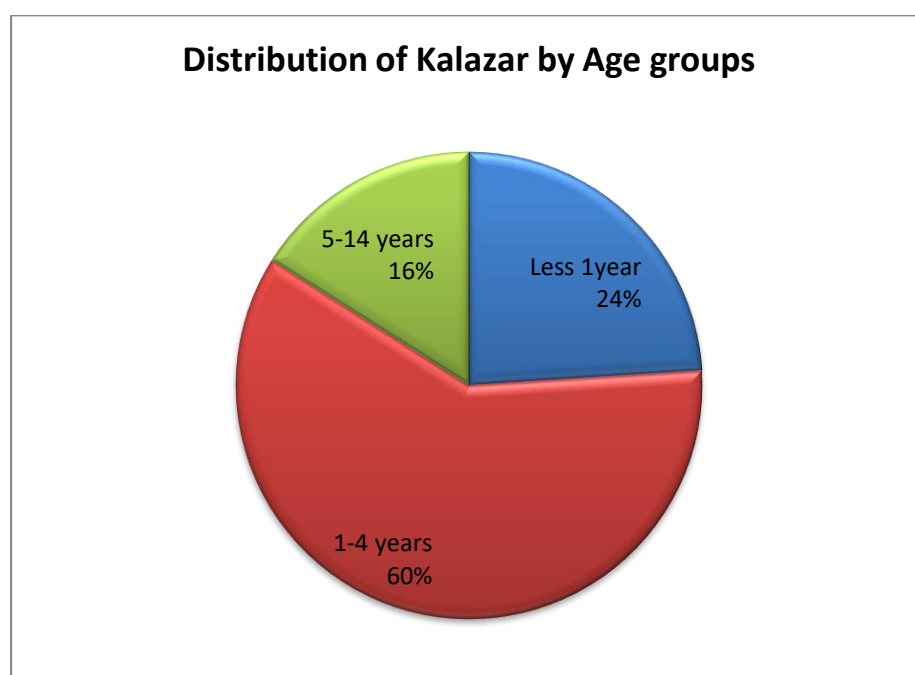


Figure 7. The distribution of cases by age group

Laboratory Diagnosis methods for examination.

The highest percentage of methods used in diagnosis are in vitro such as indirect immunofluorescence antibody (IFAT), followed by Rapid test (RAT) which is better than clinical diagnosis. Leishmaniasis can cause a wide range of clinical manifestations. Furthermore, the majority of clinical symptoms associated with leishmaniasis are not pathological. Therefore, they can mimic the pathology of other diseases that make clinical diagnosis difficult (the differential diagnosis includes, among others, infected insect bites, leprosy, tuberculosis, and melanoma for CL and malaria, African trypanosomiasis, brucellosis, and schistosomiasis). Thus, a differential diagnosis is necessary to confirm clinical suspicion. Identification of the affected *leishmania* species can be based on lymphatic clinical signs and symptoms because many species cause cutaneous and visceral swelling [25].

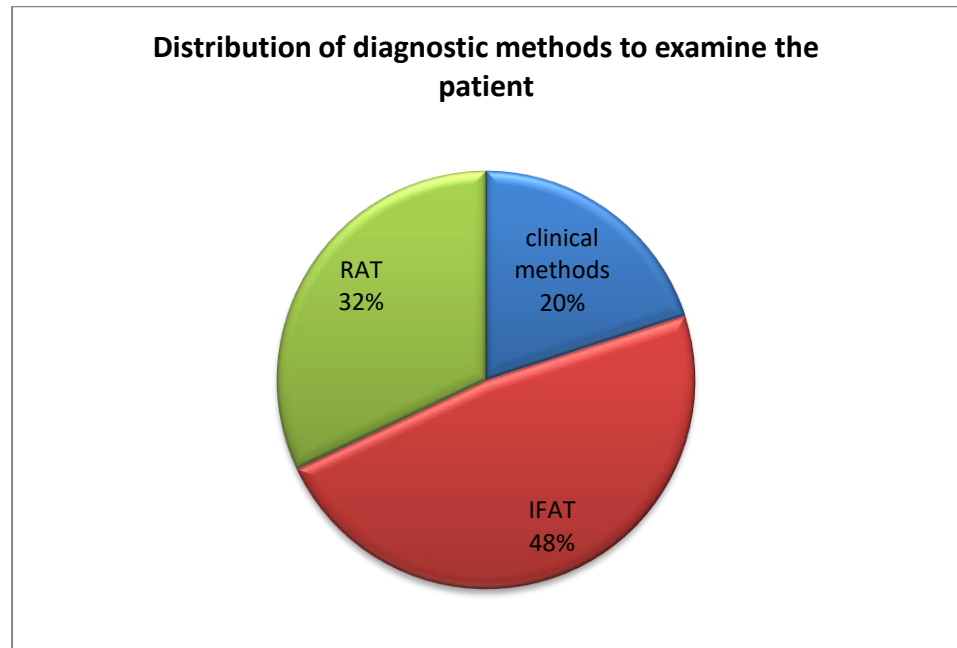


Figure 8. The ratios of diagnostic methods used to examine the patient.

Clinical symptoms of kala azar

The highest incidence of clinical symptoms was observed in anemia and splenomegaly (all twenty five patients), followed by hepatomegaly and then lymphadenopathy and fever (Fig. 9).

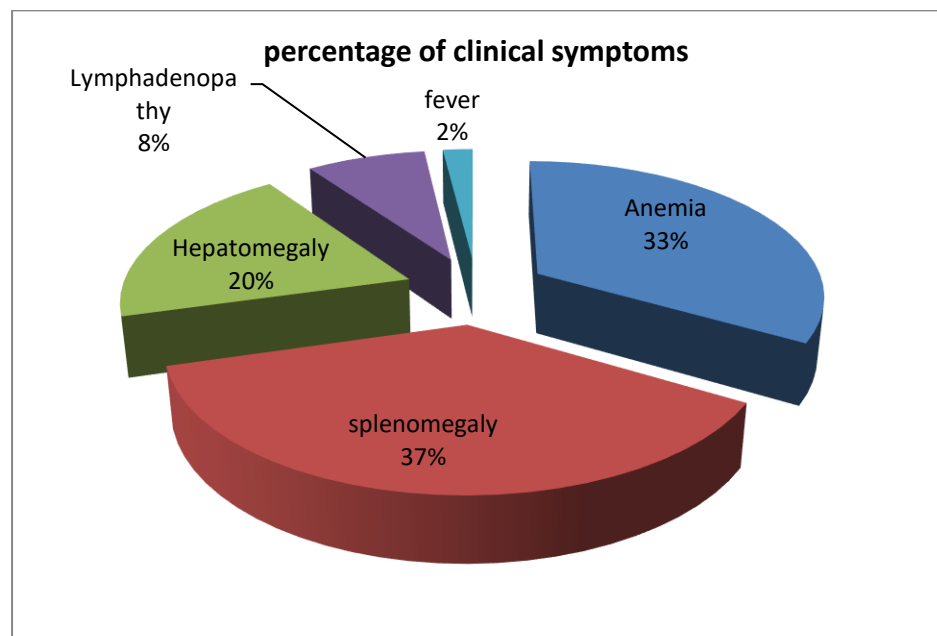


Figure 9. The percentages of cases and clinical symptoms that appeared in patients.

Final Patient Outcome

The results showed as in (Fig. 10) the cases of recovery from kalazar were higher by (80%) than the total cases, while it was 12 % for deaths in infected children. Leishmaniasis, especially visceral leishmaniasis, is still a major public health problem and a social and economic obstacle in Iraq, especially Al-Muthanna Province. The different types of Leishmania are transmitted by the bite of the sand fly. The current review proved that the incidence in southern Iraq is high and equal to the rates of injuries mentioned by some researchers for the year 2011 to 2015 [26]. The spread of leishmaniasis has increased and expanded to include most of the Iraqi governorates, especially in the south. The reason may be population growth, urban expansion, extreme poverty, and lack of health awareness. Leishmaniasis is a zoonotic disease that affects the reservoir of rodents, cats and dogs, which poses a major problem to human health. Leishmaniasis has spread in Iraq since the fifties of the last century until now, in addition to the fact that wars forced Iraqis to migrate from their governorate to other places. All this encouraged an increase in the incidence of leishmaniasis in previously uninfected areas.

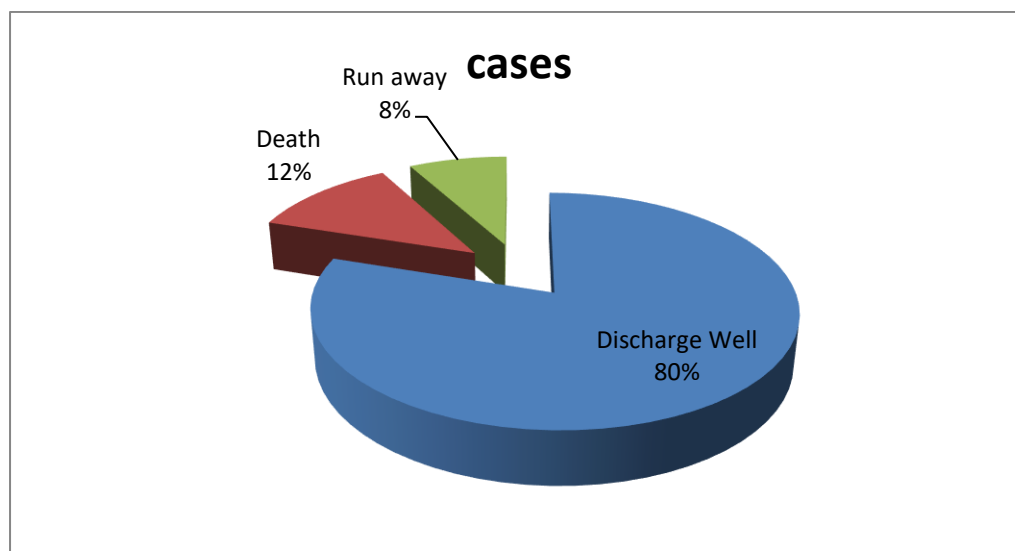


Figure 10. Represents the percentages of the final cases of patients admitted to the hospital

Conclusions

Kala azar continues to be a health care problem with a medical and social impact in the Province. The chances of infection are equal for both sexes, with a high percentage of females. The incidence of leishmaniasis is significantly higher among children in Muthanna Governorate for both sexes, compared to other age groups, while its rate decreased among older ages. The lowest infection rate was in August for all years, and the highest infection rate was in January and February. The highest cases were recorded during the winter and fall and decreased in the summer. The geographical distribution of the highest rates of kala azar was in the city of Al- Samawah, while the lowest cases were recorded in Al-Rumaitha, Khader and Al-Warka. The data also reveals the highest cases recorded in rural areas, while the lowest in urban areas. The

study proved that laboratory diagnosis is a successful and sensitive technique for detecting and identifying the *Leishmania* parasite .

Finally, kala azar or black fever is likely to affect the rural areas of Muthanna. Severe cases in children in rural areas, according to the epidemiological features of kala azar in the province, this disease is still a public health problem

Recommendations

The disease represents a serious health problem in Muthanna. Immediate attempts must be taken by governmental and non-governmental agencies to educate people about the disease and take appropriate steps to prevent and treat it. Studying the hosts of the disease in the region to get a clear vision about the transmission of the disease in addition to controlling the hosts of the parasite such as rodents and dogs, as well as spreading health awareness among the citizens. Further studies and research on sandfly, seasonal diversity of vector density, host resting sites, breeding sites, and insecticide sensitivity are urgently needed to help implement effective control measures, before leishmaniasis becomes a health burden. large in the province. Organizing epidemiological surveys, preparing a database for patients in the governorate, holding awareness seminars about the disease, and publishing posters and posters in public places, schools and health institutions. Finding techniques and rapid tests for early detection of leishmaniasis.

Conflict of Interests.

The authors declared that no competing interests exist .

Ethical Issues.

In this research, ethical considerations have been fully observed.

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Authors' Contributions.

We did write, designed the idea of the review, drafted the manuscript, and submitted the manuscript to the journal.

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