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Clinical types of cutaneous leishmanaisis In AL-IMAMAIN Alkadimain MEDICAL CITY

A thesis submitted to department of medicine / University of Al-Nahrain in partial fulfillment of the requirement for the degree of M.B.CH.B

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Abstract

Background: Leishmaniasis is widely distributed in middle east , Asia , Africa , and southern Europe and pose a major health problem and a risk for people travelling to the endemic areas.

These parasitic disease are also a problem in areas prone to displacement , war and the deterioration of living conditions and the lack or absence of health awareness.

Aim of study: to determine clinical types of cutaneous leishmaniasis in ***AL-Imamain Alkadimain medical city***

Patients and methods: Thirty patients with cutaneous leishmaniasis were included in this study, attending ***AL-Imamain AlKadimain medical city*** during the period between November 2018 till March 2019, the age range from (5 – 53) years .

RESULTS: Majority of patients in age range between 10-20 years(36.6%) . male slightly more than female. From 32 lesions, 26 lesions were dry(81.25%) and majority of infection were in face (37.5%) .

Conclusion: Dry type is most common of cutaneous leishmaniasis ,

Effect mostly age between (10-20 years) , and mostly in face

KEY WORDS: cutaneous leishmaniasis , clinical types , sand flies

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introduction

Background

Leishmanaisis is a protozoan disease caused by any of several species of *Leishmania* parasites. It is transmitted to humans and other mammals by the 2- to 3-mm blood-sucking phlebotomine sand fly. A spectrum of clinical presentations exists ranging from small nodules (tropical sore) to mucosal tissue destruction. Parasite, host, and other factors affect whether the infection becomes symptomatic and whether cutaneous or visceral leishmaniasis results. It is endemic in the tropics. The diagnosis is made clinically and may be confirmed with smears and biopsy. Cutaneous leishmaniasis may be treated with pentavalent antimonials and other drugs. Immunity to a specific species is acquired after infection.

Cutaneous leishmaniasis appears in two forms: disease found in the Middle East, Asia, Africa, and southern Europe, called "Old World leishmaniasis"; that found in Latin and Central America, called "New World leishmaniasis." Cutaneous disease is caused primarily by *Leishmania major* and *Leishmania aethiopica* in the Old World and *Leishmania mexicana* and *Leishmania braziliensis* in the New World .(1)

ETIOLOGY AND LIFE CYCLE: The genus *Leishmania* consists of parasitic protozoa of the phylum Sarcomastigophora, order Kinetoplastida, and family Trypanosomatidae. At least 21 species are pathogenic for humans and all are essentially transmitted by the bite of an infected female phlebotomine sandfly. *Leishmania* are dimorphic parasites; in the gut of the sandfly or in culture, they exist in the spindle-shaped motile (single anterior flagellum) promastigote form (10–20 ⌈m). In the cells of the host reticuloendothelial system, *Leishmania* exist in the oval nonmotile amastigote form (2–6 ⌈m) that has a relatively large basophilic nucleus and a smaller rod-shaped kinetoplast of Extranuclear DNA at the base of the lost flagellum. Infected macrophages are ingested by the fly during a blood meal and the amastigotes are released into the stomach of the insect where they immediately transform into the

promastigote form. The latter migrate to The alimentary tract of the fly, multiply extracellularly by binary fission, and in few days, reach the esophagus and the salivary glands of the fly where they change into infective metacyclic promastigotes, which will be released into the skin at next bite. They are then phagocytosed by host macrophages where they transform into amastigotes that multiply by binary fission and get released following cellular burst to infect other macrophages. (1)

RESERVOIR HOSTS :

Leishmaniasis is mostly zoonotic, being incidentally transmitted to humans from wild and domestic animals (primary reservoir hosts) However, visceral leishmaniasis (VL) caused by *Leishmania donovani* and OWcutaneous leishmaniasis (OW-CL) caused by some *Leishmania tropica* strains are anthroponotic diseases
(i.e., humans are the primary reservoir hosts).

INSECT VECTORS

The insect vector of leishmaniasis, the female phlebotomine sandfly, is grouped under the Suborder Nematocera of the order Diptera. Three genera [(1) *Phlebotomus* in the OW, and (2) *Lutzomyia* and (3) *Psychodopygus* in the NW], and around 70 species are implicated as vectors They are widely distributed and have predilection to intertropical and warm temperate zones. Only the female sandfly is
hematophagus. Phlebotomine sandflies are less than 3 mm long, and do not fly far from their breeding site. Their activity is mostly crepuscular or nocturnal while the host is asleep. They rest during the day and lay their eggs in dark, cool, humid, and organic matterrich places such as rodent burrows, bird's nests, and house wall fissures. Being exophilic and exophagic, they prefer to rest and to have their meal outdoors, which limits their control through house spraying. (2)

Epidemiology

Cutaneous leishmaniasis is endemic in Asia Minor and to a lesser extent in many countries around the Mediterranean. Iran and Saudi Arabia have a high occurrence rate.

The World Health Organization (WHO) has classified leishmaniasis as a category 1 disease (emerging and uncontrolled). The recent geographic spread is attributed to massive rural-urban migration and agroindustrial development projects that bring nonimmune urban residents into endemic rural areas. Other incriminated factors include natural disasters, cessation of malaria spraying leading to increased sandfly population, reconstructions, control programs, global warming, wars, and deforestation. Risk factors for contracting the disease include residing in an endemic area and in a ground floor, the design and construction material of the house, and the presence of domesticated animals. The prevalence of the disease increases until the age of 15 then seems to stabilize, probably reflecting development of immunity. In general, males have greater likelihood of developing the disease. This can be explained by behavioral differences in exposure as well as by hormonal modulation of disease susceptibility or resistance.(2)

PATHOGENESIS:

The resulting disease depends on the fate of the phagocytosed amastigotes. This in turn is function of numerous parasite- and host related factors, as well as other factors that may account for geographical differences In general, parasites interfere with the signaling pathways, intracellular kinases, transcription factors, and gene expression of macrophages, compromising their ability to generate leishmanicidal substances. In addition, they impair dendritic cell activation, migration, and ability to secrete T helper 1 (Th1) cytokines.(2)

Clinical features:

In Old World leishmaniasis, lesions may present in two distinct types. One is the moist or rural type, a slowly growing, indurated, livid, indolent papule, which enlarges in a few months to form a nodule that may ulcerate in a few weeks to form an ulcer as large as 5 cm in diameter. Spontaneous healing usually takes place within 6 months, leaving a characteristic scar. This type is contracted from rodent reservoirs such as

gerbils via the sandfly vector. The incubation period is relatively short (1–4 weeks). The dry or urban type has a longer incubation period (2–8 months or longer), develops much more slowly, and heals more slowly than the rural typeIn both types, the ulcer or crust forms on a bed of edematous tissue. Rarely, after the initial or “mother” lesion is healed, at the borders of the healed area, a few soft red papules may appear that are covered with whitish scales and have the “apple jelly” characteristics of granulomatous diseases such as lupus vulgaris. These spread peripherally on a common erythematous base and are the lupoid type. This is also known as leishmaniasis recidivans and occurs most often with the urban type of disease, caused by *Leishmania tropica.* New World disease may also induce purely cutaneous lesions, of varied morphology. The primary papule may become nodular, verrucous, furuncular, or ulcerated, with an infiltrated red border Subcutaneous peripheral nodules, which eventually ulcerate, may signal extension of the disease. A linear or radial lymphangitic (sporotrichoid) pattern may occur with lymphadenopathy, and the nodes may rarely yield organisms. Facial lesions may coalesce and resemble erysipelas.(3)

Histopathology

An ulcer with a heavy infiltrate of histiocytes, lymphocytes, plasma cells, and polymorphonuclear leukocytes is seen. The parasitized histiocytes form tuberculoid granulomas in the dermis. Pseudoepitheliomatous hyperplasia may occur in the edges of the ulcer. Leishmanias are nonencapsulated and contain a nucleus and a paranucleus. Wright, Giemsa, and monoclonal antibody staining may be helpful in identifying the organisms within histiocytes, where they often line up at the periphery of a vacuole. Polymerase chain reaction primers are available for a variety of species. PCR is more sensitive than microscopy but

less sensitive than culture(3)

Diagnosis

In endemic areas, the diagnosis is not difficult. In other localities, cutaneous leishmaniasis may be confused with syphilis, yaws, lupus vulgaris, and pyogenic granulomas. The diagnosis is established by demonstration of the organism in smears. A punch biopsy specimen from the active edge of the ulcer is ideal for culture. It can be placed in Nicolle-Novy-MacNeal (NNN) medium and shipped at room temperature. Parasites can also be cultured from tissue fluid. A hypodermic needle is inserted into the normal skin and to the edge of the ulcer base. The needle is rotated to work loose some material and serum, which is then aspirated. A culture on NNN medium at 22–35°C (71.6–95°F) is recommended to demonstrate the leptomonads. As expected, PCR is the most sensitive diagnostic test for cutaneous leishmaniasis.(3)

Treatment

Spontaneous healing of primary cutaneous lesions occurs, usually within 12–18 months, shorter for Old World disease. Reasons to treat a self-limited infection include avoiding disfiguring scars in exposed areas, avoiding secondary infection, controlling disease in the population, and failure of spontaneous healing. In the diffuse cutaneous and recidivans types, leishmaniasis may persist for 20–40 years if not treated. In areas where localized cutaneous leishmaniasis is not complicated by recidivans or sporotrichoid forms or by mucocutaneous disease, treatment with such topical modalities as paromomycin sulfate 15% plus methylbenzethonium chloride 12%, ketoconazole cream under occlusion, cryotherapy, local heat, photodynamic therapy, and laser ablation, or with intralesional sodium stibogluconate antimony or emetine hydrochloride may be effective and safe. In the setting of Old World cutaneous leishmaniasis, some data suggest that intramuscular meglumine antimoniate in combination with intralesional meglumine antimoniate may be superior to intralesional therapy alone.

Oral fluconazole and zinc sulfate have been used to treat *Leishmania major* infection.
In immunosuppressed patients or those who acquire infection in areas where mucocutaneous disease may occur, systemic therapy is recommended. As with topical treatment, many alternatives have been reported to be effective. Sodium antimony gluconate (sodium stibogluconate) solution is given intramuscularly or intravenously, 20 mg/kg/day in two divided doses for 28 days.
Other systemic medications reported to be effective include fluconazole (200 mg/day for 6 weeks), ketoconazole, dapsone, rifampicin, and allopurinol.(3)

Prevention and control:

No vaccines or drugs to prevent infection are available. The best way for travelers to prevent infection is to protect themselves from sand fly bites. To decrease the risk of being bitten, follow these preventive measures. Avoid outdoor activities, especially from dusk to dawn, when sand flies generally are the most active.

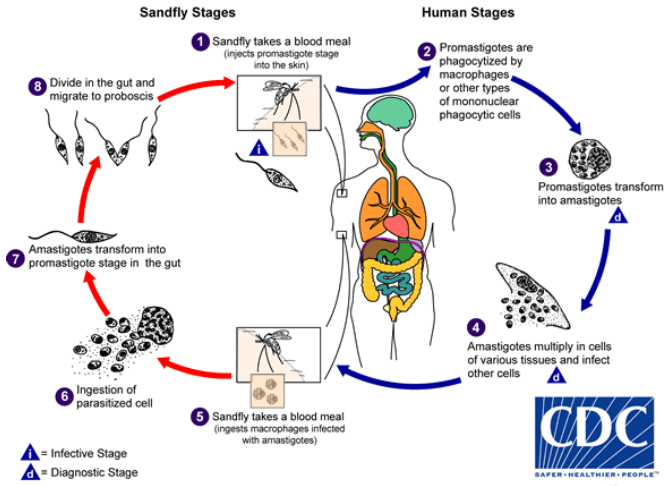
When outdoors (or in unprotected quarters)**:**

- Minimize the amount of exposed (uncovered) skin. To the extent that is tolerable in the climate, wear long-sleeved shirts, long pants, and socks; and tuck your shirt into your pants .Apply insect repellent to exposed skin and under the ends of sleeves and pant legs. Follow the instructions on the label of the repellent. The most effective repellents generally are those that contain the chemical DEET (N,N-diethylmetatoluamide).

When indoors**:**

- Stay in well-screened or air-conditioned areas.
- Keep in mind that sand flies are much smaller than mosquitoes and therefore can get through smaller holes.

- Spray living/sleeping areas with an insecticide to kill insects.
- If you are not sleeping in a well-screened or air-conditioned area, use a bed net and tuck it under your mattress. If possible, use a bed net that has been soaked in or sprayed with a pyrethroid-containing insecticide. The same treatment can be applied to screens, curtains, sheets, and clothing (clothing should be retreated after five washings).(4)



life cycle of leishmanaia

dry type

Wet type

phlebotomine sandfly

Aim of study:

Determine clinical types of cutaneous leishmaniasis In Al-Imamain Alkadimain medical city

Patients and method

Thirty patients with cutaneous leishmaniasis were included in this study, attending ***AL-Imamain AL-Kadimain medical city*** during the period between November 2018 till March 2019, the age range from (5 – 53) years. They were diagnosed depending on clinical picture by dermatologist . All the individuals were subjected to questionnaire about Name , Age , Sex , residency , occupation , Travel and Family history , Also there chief complaint , Duration , Number of lesions , Site , Type , Presence of secondary infection .

Type of study*: cross-sectional study*

Statistical analysis: *percentage*

Results

30 patients were included in this study

There was 17 males (56%) and 13 females (44%)

Regarding the age , the patient who are between 10 years and 20 years were the mostly effected n=11(36.6%) then the age below 10 years n=8(26%) then ages between 20 to 30 and the age between between 30-40 and the age between 50-60 has equal incidence n=3(10%) each one of them. The least was in the age between 40 years and 50 years n=2(6.6%)
Regarding residency, most of the patients live in rural areas n=18(60%) and the remaining live in urban areas n=12(40%)

Regarding the family history , most of the patient have negative family history n=24(80%) . and only n=6(20%) have positive family history

Regarding the travel history , most of the patients have negative travel history n=20(66.6%) and remaining n=10 (33.3%) have positive travel history

Regarding chief complaint , most of the patients complaint from disfigurement n=19(63.3%) followed by pain n=7(23.3%) and least complaint is itching n=4(13.3%)

Regarding the type of lesions , it was mostly dry in 26 patients(81.25%) and wet in patients 6 patients (18.75%)

Regarding presence of secondary bacterial infection , it was negative in lesions n=20(62.5%) , and positive in lesions n=12(37.5%)

Regarding number of lesions patients have one lesion n=28(93.33%) and others have 2 lesions n=2(6.66%)

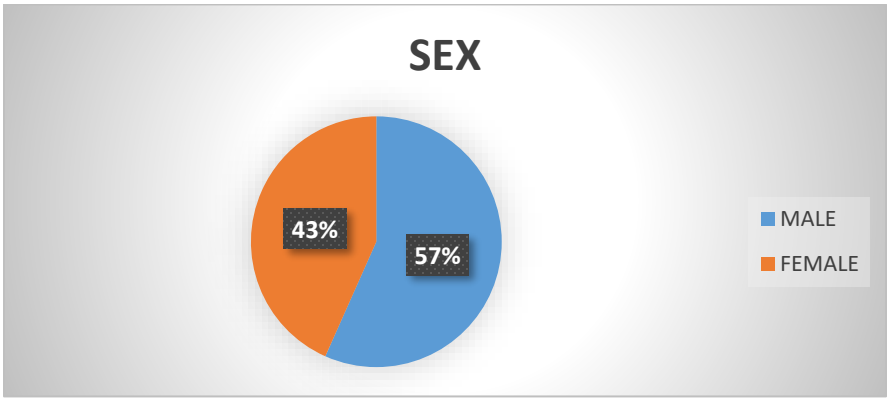
Regarding the site , some patients have more than one site involved in the disease and the result show that the face is mostly effected n=12(37.5%) followed by abdomen n=8(25%) ,foot n=4(12.5%) followed by hand n=3(9.375%) ,arm and leg n=2(6.25%) each one of them and least site is neck n=1(3.125%)

Results:

Table(1) : Distribution of patients according to sex

SEX	FREQUENCY	PERCENT
MALE	17	56
FEMALE	13	44
TOTAL	30	100

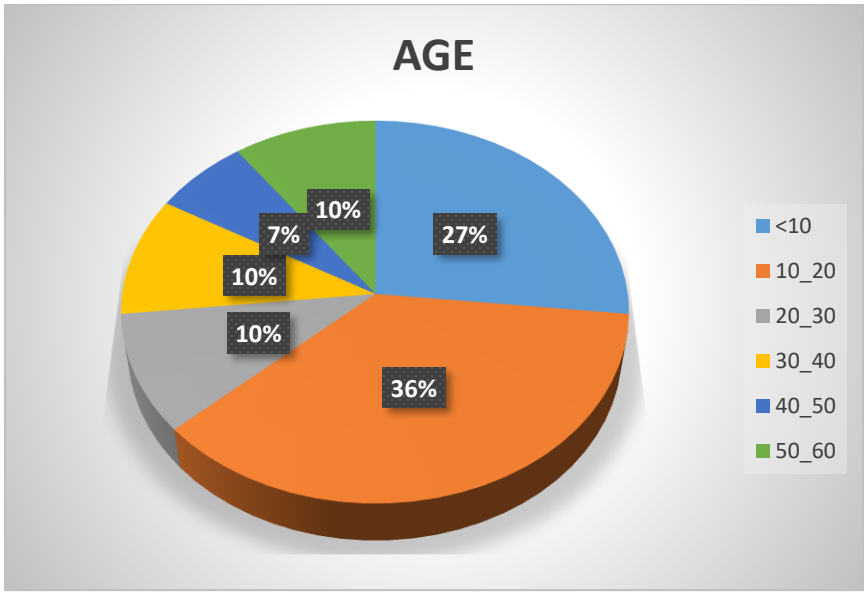
Figure(1) : Distribution of patients regarding sex



Table(2) : Distribution of patients regarding age

AGE	FREQUENCY	PERCENT
<10 years	8	26
10_20 years	11	36.6
20_30 years	3	10
30_40 years	3	10
40_50 years	2	6.6
50_60 years	3	10

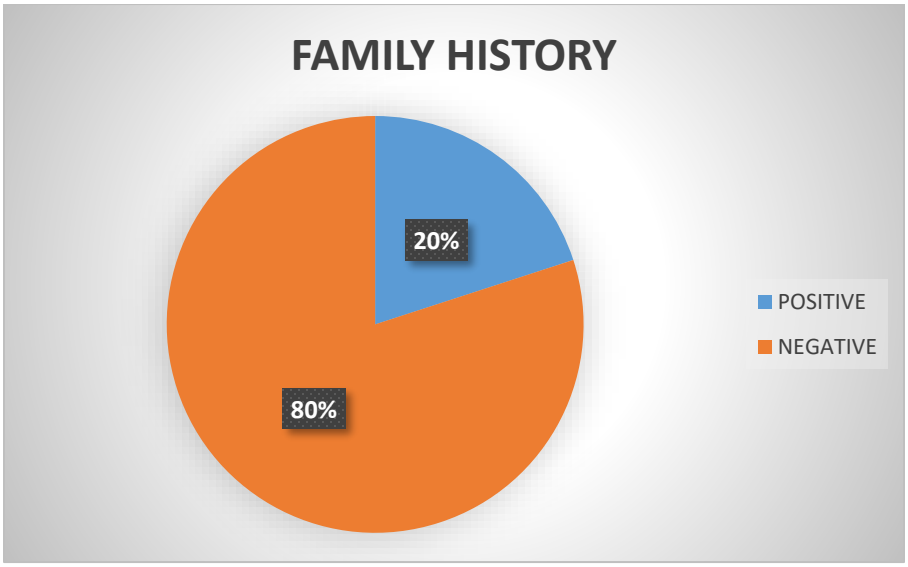
Figure(2) : Disribution of patients regarding age



Table(3) : Distribution of patients regarding family history

FAMILY HISTORY	FREQUENCY	PERCENT
POSITIVE	6	20
NEGATIVE	24	80
TOTAL	30	100

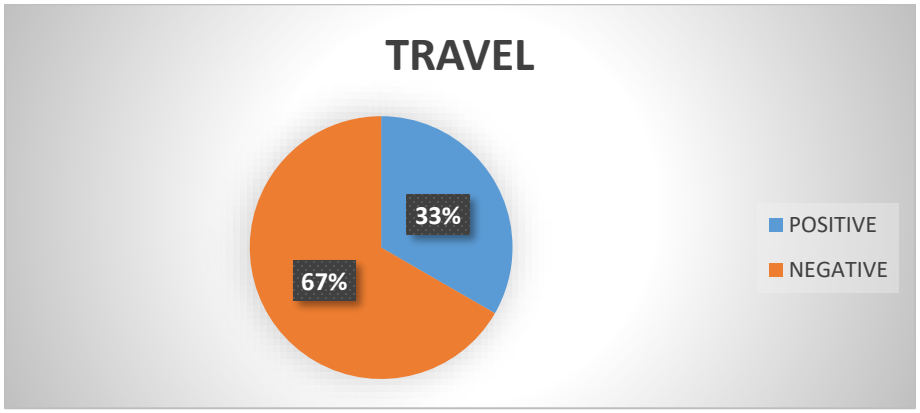
Figure(3) : Distribution of patients regarding family history



Table(4) : Distribution of patients according to travel history

TRAVEL	FREQUENCY	PERCENT
POSITIVE	10	33.3
NEGATIVE	20	66.6
TOTAL	30	100

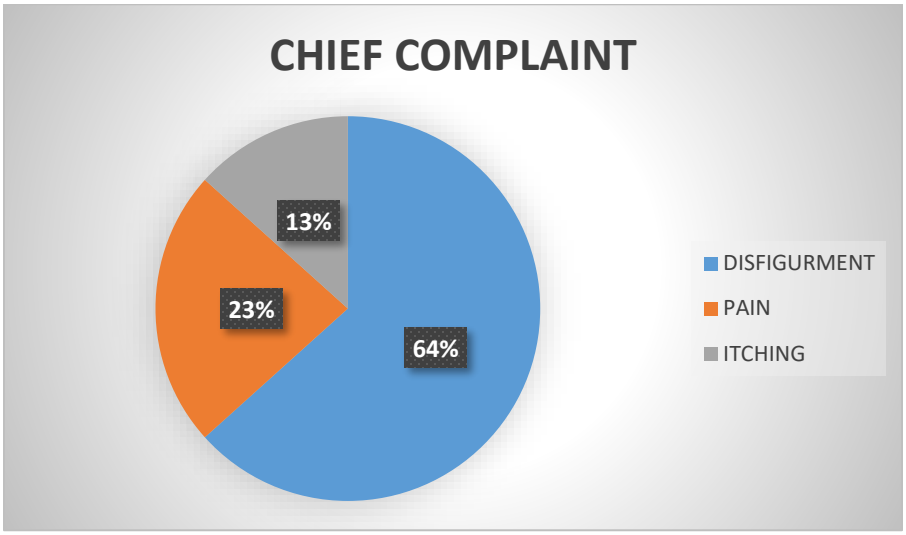
Figure(4) : Distribution of patients according to travel history



Table(5) : Distribution of patients according to their chief complaint

CHIEF COMPLAINT	FREQUENCY	PERCENT
DISFIGURMENT	19	63.3
PAIN	7	23.3
ITCHING	4	13.3
TOTAL	30	100

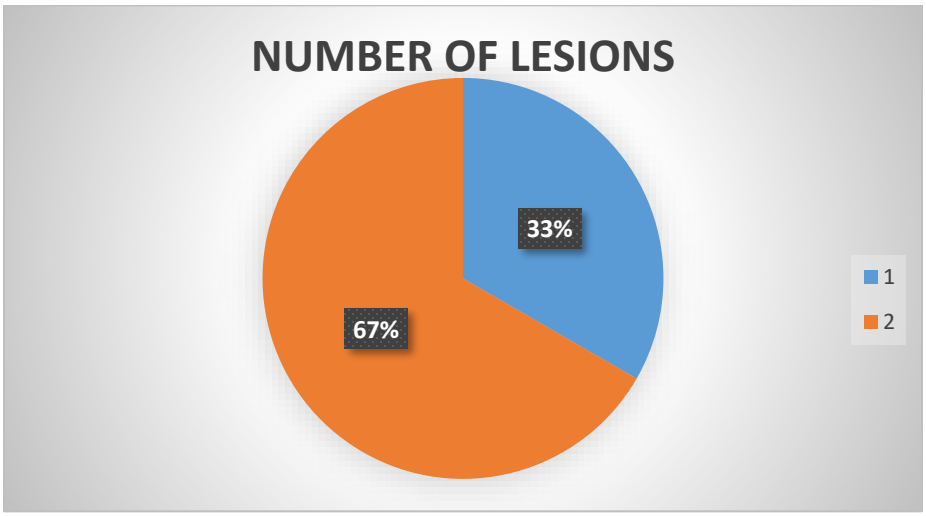
Figure(5) : Distribution of patients according to their chief complaint



Table(6) : Distribution of patients according to number of lesions

NUMBER OF LESIONS	FREQUENCY	PERCENT
1	28	93.33
2	2	6.66

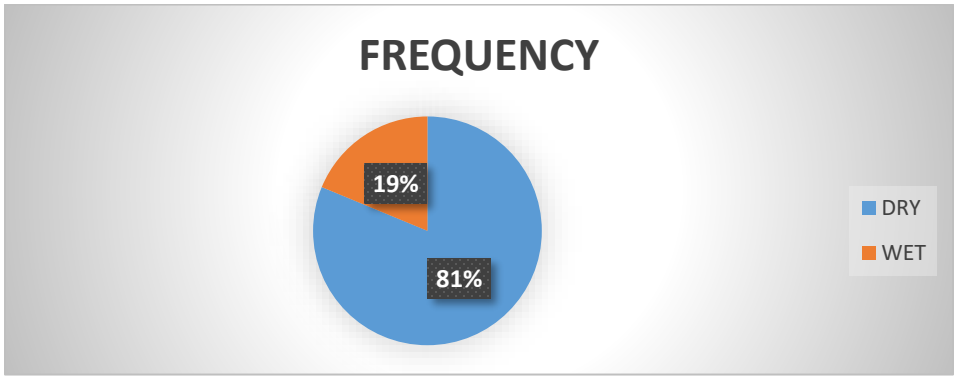
Figure(6) : Distribution of patients according to number of lesions



Table(7) : Distribution of lesions according to type

TYPE	FREQUENCY	PERCENT
DRY	26	81.25
WET	6	18.75
Total lesions	32	100

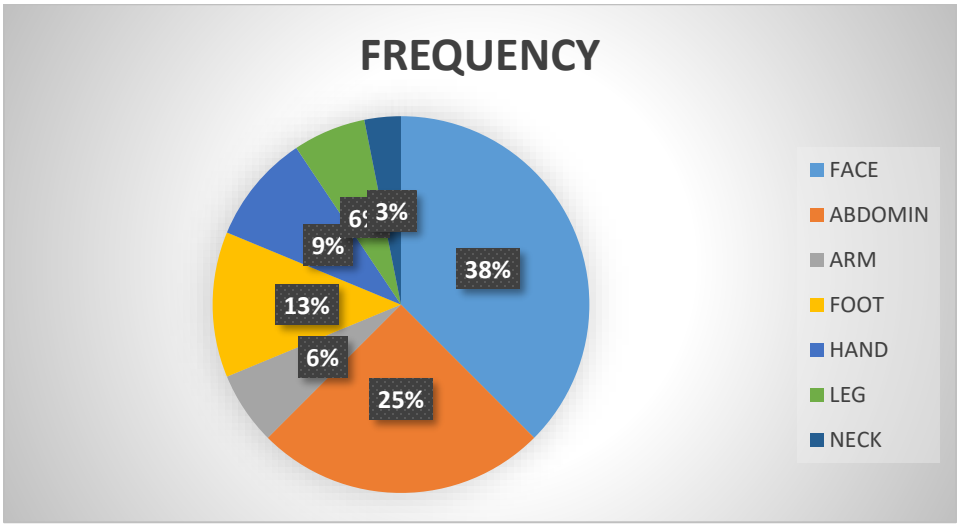
Figure(7) : Distribution of lesions according to type



Table(8) : Distribution of lesions according to site

SITE	FREQUENCY	PERCENT
FACE	12	37.5
ABDOMIN	8	25
ARM	2	6.25
FOOT	4	12.5
HAND	3	9.375
LEG	2	6.25
NECK	1	3.125
TOTAL	32	100

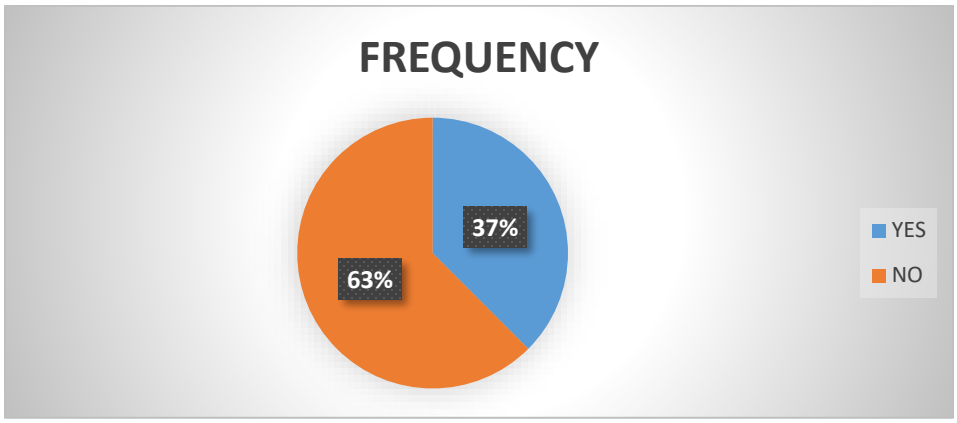
Figure(8) : Distribution of lesions according to site



Table(9) : Distribution of lesions according to presence of secondary infection

SIN	FREQUENCY	PERCENT
YES	12	37.5
NO	20	62.5
Total lesions	32	100

Figure(9) : Distribution of lesions according to presence of secondary infection



Disscussion

Leishmaniasis is a parasitic disease caused by haemoflagellates belonging to the genus leishmania ,the infection is transmitted to humans through the bites of female phlebotomine sandflies(5).. Leishmaniasis is prevalent in many parts of the world especially tropical and subtropical countries. Two million new cases of leishmaniasis occur each year. Both visceral and cutaneous forms of the disease occur in the Mediterranean region and there clinical features vary from each other(6) . leishmaniasis is endemic in Iraq with the visceral form of the disease ,caused by L.donovani complex, is mainly endemic in central parts of the country.in contrast,the cutaneous form, caused by L.tropica or L.major , is more wide spread(7). Increase outbreaks of the disease occurred in Iraq in recent years(8)

This study included 30 patients with cutaneous leishmaniasis , the range was (5 – 53) years , the mean age of CL patients was 20.8 years , and the peak of incidence 36.6% was at the age group (10 – 20) years which is consistant with study done by *Mishri Lal Khatri MD, Nasser Haider* 2001 and study done by Sezen kocarslan , enver turan , turan ekinci , rabia apari (9,10)

But unconsistant with (11 , 12 ,13) which show that most common age was (20 – 30) this high rate of infection amoung this age could be low poor families , with poor healthy hygiene , outdoor activities .

Regarding the gender this study found that the propotion of males was slightly higher than females , this mean that the disease could effect both sexes , this may be due to low number of sampling and in both male and female sex.

Most patients of CL came from urban and rural areas surrounding Baghdad , indicate that this area may be endemic by leishmaniasis , many factors can play an important role in distribution of the disease in this area , including the presence of animals resevoirs like rodents and dogs , using the open building which harbours many kinds of insects and which is close to the population . these results agreed with (14 and 15) , as well as agreement with Camargo L.B.(2006)(16) IN Brazil who reported that the presence of animals resevoirs such as foxes , dogs , and marsupials , play an important role in the presence and distribution of leishmaniasis.

According to disease behavior , our data showed that 26(81.25%) of patients had dry type , followed by 6(18.75%) wet type , the result of AL-Aubaidi (17) and AL-Diwany (18) disagree with our results and also similar study by (Abdulsadah A R 2014 (19)) in Kut city , where the wet type was higher(61%) than dry type (39%) the reasons could be caused by the influence of sample size , patient selection and host immune response.

Most of the lesions were found on the the face n=12(37.5%) this result agree with(20,21,22,23) , all these patients had disfigurement complaint because the face is exposed site ,this result differ from AL_Obaidhi(2000)(24) that found CL lesions occurred mainly on upper limbs and lower limbs , less frequently on the face .

Regarding chief complaint of the patient . Most patients complaint from disfigurement n=19(63.3%) followed by pain n=7(23.3%) followed by itching n=4(13.3%) , this result agreed with(25) .

In this study the number of lesions ranged from 1 – 2 , these results disagree with (26 - 27) which show that the number of lesions ranged from (1 – 3) may be due to low number of samples .multiple lesions are

due to repeated and to phlebotomine sand flies and high population density of sand flies in this area.

Conclusion

1-Dry type is most common type of cutaneous leishmaniasis

2-Effect mostly age between (10-20 years) , and mostly in face

Recommendation

1-use of topical antiseptic solution are needed for wet type lesions to prevent secondary bacterial infection and prevent tissue distruction , use of antibiotic against Staphylococcus would be logical

2-homes,schools purification of insects , specially in endemic area and clearance from recervoirs(dogs , rodents) to prevent coexistence with insect

Questionnare form

Name:

Age:

Sex:

Occupation:

Travel:

Residency:

Family history:

Chief complaint:

Duration:

Number of lesions:

Site:

Type:

Secondary bacterial infection:

Refrences

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