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Epidemiology, Pathology and Treatment of Cutaneous Leishmaniasis in Makah Region of Saudi Arabia 2023

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Abstract:

Background:

Leishmaniasis is a parasitic infection endemic in more than ninety countries of the world. The (CL) is a most common form of leishmaniasis and it remains to be a major public health issue in Saudi Arabia. (CL)is an annoying and disfiguring disease affecting around 1,500,000 individuals globally. There are endemic pockets of this disease in Saudi Arabia. In some patients, lesion often weeps and leads to scar formation. Leishmaniasis is infectious disease. It is an intracellular parasitic microorganism that develops in the body of infected female phlebotomine sandflies vector, prior to its transmission to human or animal host by the vector bite. CL is a vector-borne protozoan infection affecting a large number of people in several countries, around 1.5 million CL new cases are emerging annually and approximately 350 million people are at risk. The great number of CL cases occurs in Algeria, Brazil, Afghanistan, Iran, Peru, Syria and Saudi Arabia.

Aim of the study: To highlight the current the epidemiology, pathology and treatment of CL in Makah Region of Saudi Arabia 2023.

Methods: Across sectional descriptive study conducted among patients visiting the primary health care in Makah region at Saudi Arabia, during the February to April, 2023, the Sample size of patients affected by Cutaneous Leishmaniasis our total participants were (60).

Results: shows that the majority of participants approximately (30.0%) were aged from 31-40 years, regarding sex, more than half of participant (53.33%) were , regarding living environment the majority of participant far from farms/no plants inside houses were (66.67%), regarding employment status most of participants employed were (70.0%), regarding the

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location of lesions the majority of participant head, face, and neck were (45.0%) regarding number of lesions most of participants from 3–4 were (40.0%) while 1-2 were (31.67%), regarding the residence the majority of participant urban were (81.0%) followed by rural were (19.0%), regarding animals around house most of participants answer No were (51.67%). **Conclusion:** Transmission of leishmaniasis in Makah region is probably because of poor coverage of residual insecticides spraying at hiding places in pile-ups of rocks and abandoned houses from where sand flies visit nearby houses and cattle sheds during night. Fluconazole and itraconazole may be used for the treatment of CL with good recovery rate and fewer side effects

Keywords: epidemiology, pathology, treatment, Cutaneous Leishmaniasis , Makah, Saudi Arabia, primary health care .

Introduction

Leishmaniasis is a parasitic infection endemic in more than ninety countries of the world and the (CL) is a most common form of this infection caused by phlebotomine sand fly [1]. The World Health Organization reported in 2016 that about 15million individuals have leishmaniasis and more than 360 million individuals are breathing in those regions which are prone for this infection and this infection causes ~ 70,000 deaths per year [2]. It is now well documented that Cutaneous Leishmaniasis is caused by more than 22 different species of the genus Leishmania (L) but their prevalence varies from region to region [3]. Identification of specific Leishmaniasis species is important for the prescription of appropriate therapy [4]
Additionally, some patient with (CL) present late to health services with severe unwanted complications, such as large ulcerative crusted nodules, nasal deformities, disfigured lips, large scars, or even malignant transformations.[5]. (CL) social stigma (CLSS) significantly impacts the lives of affected individuals, including their social interactions, marriage prospects, and the ability to find employment. Unfortunately, patient with (CL) are particularly victimized as they are considered unacceptable for marriage and are sometimes no longer accepted by their own families.[6] Many research studies have shown that the stigma and discrimination associated with (CL) can negatively impact emotional well-being and mental health.[7] People living with (CL) start to see themselves in a negative light due to the stigma they experience, which can lead to feelings of anxiety and depression. Furthermore, they may also be afraid of discrimination or judgment if others find out about their condition [8]

Diagnosis of Cutaneous Leishmaniasis is usually done through demonstration of the leishmanial parasite in skin smears or biopsy with direct microscopy-based detection methods that commonly lack sensitivity and specificity [9]. Several PCR-based assays that allow both parasite detection and species identification, with a high degree of sensitivity and specificity, have been developed [10]. (CL) skin lesions are often self-healing, but sometimes mandate treatment. The pentavalent antimonial medications remain the standard treatment in many parts in the world [11]. Nonetheless, these compounds are frequently blamed for their serious side-effects and the reported possibility of treatment failure, resistance and skin lesions relapse [12]

As far as the treatment is concerned, it includes thermotherapy, cry therapy, surgical excision and chemotherapy.[13] Most commonly used agents are antimonial compounds, amphotericin-B, ketoconazole and itraconazole [14]. However, due to high toxicity associated with

pentavalent antimonial compounds and emergence of drug resistance; combination therapy using liposomal Amphotericin- B with pentamidines or miltefosine has also been tried as a better alternative[15] . Fluconazole has also been tried in different dosage in recent past with success for the treatment of (CL) caused by Leishmania major [16]. Cutaneous leishmaniasis when not treated promptly causes disfiguring, resulting into social stigma particularly among women and, therefore, must be eradicated.[17]

Saudi Arabia which is a tropical country has endemic pockets of (CL) in Al-Hassa, Al-Gaseem, Madina, Hail, Riyadh, Asir, Tabooq, Taif, Al-Baha, Jazan, Najran and Bisha. Lots of cases were detected in Asir, Al-Baha, Arar, El-Quassim and Riyadh provinces[18,19]. Leishmaniasis. tropical is in abundance in foothills of the Asir range in the south-west of Saudi Arabia [20]. Both Leishmaniasis major and L. tropical were found in Al-Baha and Al-Qasim in the western region of the kingdom[21]. Recently, incidence of these species has increased in other countries like Egypt, Iran and Israel [22]. Similar increases have also been reported in the density of Phlebotomize papatasi and P. sergenti which increased the risk of (CL) transmission in Asir and Medina Munawwara [23]

Literature Review

In earlier studies, Phlebotomies papatasi was incriminated as vector for Leishmania major in Al-Hassa oasis and Riyadh provinces of Saudi Arabia [24]

In a study, carried out in southeastern Tunisia, most of the cases were recorded in the summer [25]. The local climate and its effects on the host-vector activities could explain seasonality variations among different studies [26]

All CL lesions were confined to the skin with no mucosal tissue involvement or nodular dissemination noticed in all cases, consistent with previous studies and inconsistent with others [27]

We reported positivity rate as 0.29% which is much less than that reported as 5.5% in Southern Jordan valley and 10% in Shah rood district, Central Iran [28]

Health statistical year books of MOH, Saudi Arabia for 2007-2009 showed 41, 45 and 31 cases of cutaneous leishmaniasis in Taif region [18]

Amin et al (2013) report that progress made in disease's diagnosis and the increase in population's awareness towards the value of early treatment may be additional explanations. Taken together, it was clear that Cutaneous leishmaniasis in the study setting is more frequent than perceived in the literature and mandate further attention from the health authorities. Cutaneous leishmaniasis cases were reported all the year around, but most of the cases were reported in the winter, in agreement with previous Saudi studies [29] . During 2013, 27 cases of (CL) were recorded from this region which is little less than what was reported in 2009. These data clearly indicates the establishment of sand flies in Taif region. It is probably because of varied type of breeding and hiding places which are really difficult to approach. Though control program is taking care of destroying Leishmania vector specially by fogging of infested areas, it seems that it is not helping much as most of the sand flies during fogging remain in their hiding places like spaces under the big rocks which are numerous and could not easily be approached. Synthetic pyrethroids such as deltamethrin, cyfluthrin and lambdacyhalothrin as

residual insecticides had already been used to control sand fly population with great success in many Leishmania infested countries including Moracco and Iran [30]

Rationale:

Despite the great efforts by health authorities in Kingdom of Saudi Arabia (KSA), (CL) continues to be a major public health problem in the country. Many risk factors make KSA prone to outbreaks and epidemics; among these, rapid urbanization and the huge population movement are the most important. The disease is endemic in many parts of KSA, with the majority of cases concentrated in six regions, including Al-Qaseem, Riyadh, Al-Hassa, Aseer, Ha'il, and Al-Madinah. Transmission of leishmaniasis in Makah region is probably because of poor coverage of residual insecticides spraying at hiding places in pile-ups of rocks and abandoned houses from where sand flies visit nearby houses and cattle sheds during night, this is the first comprehensive study that shows the majority of leishmaniasis in Makah region was caused by L. major and L. tropica. This requires higher alert to the Ministry of Health of Saudi Arabia to take proactive actions in preventing the onset of L. major, L. tropica, L. infantum and L. donovani infections

Aim of the study:

To highlight the current the epidemiology, pathology and treatment of Cutaneous Leishmaniasis in Makah region of Saudi Arabia 2023 .

Objectives:

To highlight the current the epidemiology, pathology and treatment of Cutaneous Leishmaniasis in Makah region of Saudi Arabia 2023 .

Methodology:

Study design:

This study is a cross-sectional study design was used in carrying out of this study.

Study Area

The study will be carried out in the Makah region at Saudi Arabia is the holiest spot on Earth. It is the birthplace of the Prophet Mohammad and the principal place of the pilgrims to perform Umrah and Hajj. It is located in the western area in Kingdom of Saudi Arabia and called the Holy Capital. Contains a population around 2.578 million. The study was conducted on the patients attending the hospitals located in proposed areas with the help of paramedical staff deputed there and Communicable Diseases Control Centre, MOH, Makah at Saudi Arabia, and it reflects a diversified demographic profile with a considerable portion of the population comes from rural descent, while others come from an urban one. This difference translates into biological, socioeconomic and lifestyle differences in the population.

Study Population

The study was conducted on the patients attending the hospitals located in proposed areas with the help of paramedical staff deputed there and Communicable Diseases Control Centre, MOH, Makah at Saudi Arabia regarding the epidemiology, pathology and treatment of Cutaneous Leishmaniasis in Makah region in Saudi Arabia 2023, among patients attending the hospitals located in proposed areas with the help of paramedical staff deputed there and Communicable Diseases Control Centre, MOH, Makah at Saudi Arabia , who aged from <10 years - > 41 years and their total number was (60)

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Selection criteria:

Inclusion criteria

- Positivity of Leishmania was recorded by microscopic examinations
- aged from <10 to >41 year
- male and female

Exclusion criteria :

- No specific exclusion criteria.

The sample size

The sample size has been calculated by applying Raosoft sample size calculator based on (The margin of error: 5%, Confidence level: 95%, and the response distribution was considered to be 20%) accordingly to sample size from medical practitioners by the required sample size; (60). (male and female) and adding 10 more to decrease margin of error. After adding 5% oversampling, the minimum calculated sample has been 60. Computer generated simple random sampling technique was used to select the study participants. Data collection was done by the researcher during the February to April , 2023 .

Sampling technique:

Systematic random sampling technique is adopted. After that, by using random number generator, then simple random sampling technique was applied to select the visiting the primary health care. Also convenience sampling technique will be utilized to select the participants in the study. By using systematic sampling random as dividing the total patients attending in the Primary health care by the required sample size; (60).

Data collection tools of the study:

Patients were interviewed with structured questionnaire. Tool was designed to collect the necessary data, and developed by the researchers after review of the literature .

Tool I: In hospitals located in proposed areas with paramedical staff deputed there and Communicable Diseases Control Centre, MOH, Makah at Saudi Arabia through structured interview questionnaire, the questionnaire comprised :

First part: Information about the patient's socio- demographic features (age, gender, residence, nationality, animals in or near the house and leishmaniasisendemic areas visited 1-2 months before eruption of the skin lesions).

Second part: Information about the patient's medical history (prior medications, home remedies, concomitant diseases and lesion's evolution time):

The lesion's evolution time was calculated by the time interval from the lesion's eruption day till the patient's consultation day. The clinical examination involved tissue-affected, lesion characteristics (number, size, site and appearance), for patients with multiple lesions, the surface area was reported as a mean size of the total lesions .

Data collection technique:

Researcher has be visits the selected the hospitals located in proposed areas, after getting the approval from the ministry of health and participants. After the arrival of the participants has be explained the purpose of the study to all participants attending with the help of paramedical staff deputed there and Communicable Diseases Control Centre, MOH, Makah, the present study on cutaneous leishmaniasis was conducted in in Makah region where a few endemic pockets are available such as Turbah, Al-Garya, Missan and Hadad. These places were selected

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as they had varied ecological conditions, from sandy and rocky to bushy and hilly terrain. Main focus of the study was epidemiological and pathological aspects of the disease along with vector control .

Data entry and analysis:

The Statistical Package for Social Sciences (SPSS) software version 24.0 will be used for data entry and analysis. Descriptive statistics (e.g., number, percentage) and analytic statistics using Chi-Square tests ($\chi 2$) to test for the association and the difference between two categorical variables were applied. A p-value ≤ 0.05 will be considered statistically significant.

Pilot study

A pilot study has be conducted in selected the hospitals located in proposed areas, after getting the approval from the ministry MOH, Makah , using the questionnaire to test the methodology of the study. As a feedback, the questionnaire will be clear and no defect has be detected in the methodology

Ethical considerations

Permission and approval from the ministry MOH, Makah and the hospitals has be obtained. Permission from the Directorate of health , verbal consents from all participants in the questionnaire were obtained. All information was kept confidential, and a result has be submitted to the department as feedback .

Budget: Self-funded

Result

Table 1. Distribution of the Socio-demographic characteristics of participants (n = 60).

	N	%
Age		
10–20	18	30.00
21–30	15	25.00
31–40	18	30.00
≥41	9	15.00
Sex		
Female	28	46.67
Male	32	53.33
Living environment		
Inside or nearby farms/multi-planted houses	20	33.33
Far from farms/no plants inside houses	40	66.67
Marital states		
Married	27	45.00
Single (did not experience marriage)	18	30.00
Single (separated, divorced, widow)	15	25.00
Employment status		
Children/students/no jobs	18	30.00

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Employed	42	70.00
Location of lesions		
Head, face, and neck	27	45.00
Upper extremities	13	21.67
Lower extremities	20	33.33
Educational level		
Uneducated or primary school	13	21.67
Intermediate + secondary schools	25	41.67
Higher education (University Graduates)	22	36.67
Number of lesions		
1–2	19	31.67
3–4	24	40.00
≥5	18	30.00
Residence		
Rural	11.4	19.00
Urban	48.6	81.00
Travel history		
Yes	26	43.33
No	34	56.67
Animals around house		
Yes	29	48.33
No	31	51.67
Nationality		
Saudi	53	88.33
Non-Saudi	7	11.67

This table 1 shows that the majority of participants approximately (30.0%) were aged from 31-40 years and 10-20 years of age, while age from 21-30 years were (25.0%) followed by ≥41 years were (15.0%), regarding sex, more than half of participant (53.33%) were male followed by female were (46.67%), regarding living environment the majority of participant far from farms/no plants inside houses were (66.67%) followed by inside or nearby farms/multi-planted houses were (33.33%), regarding marital status, the majority of participant (45.0%) were married followed by single (did not experience marriage) were (30.0%) while Single (separated, divorced, widow) were (25.0%), regarding employment status most of participants employed were (70.0%) followed by children/students/no jobs were (30.0%), regarding the location of lesions the majority of participant head, face, and neck were (45.0%) followed by lower extremities were (33.0%) while upper extremities were (21.67%), regarding the educational level, this table reveals that approximately of participant intermediate + secondary schools were (41.67%) while higher education (University Graduates) were (36.67%) while uneducated or primary school were (21.67%), regarding number of lesions most of participants from 3–4 were (40.0%) while 1-2 were (31.67%) followed by >5 were (30.0%), regarding the

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residence the majority of participant urban were (81.0%) followed by rural were (19.0%), regarding the travel history most of participant answer No were (56.67%) while answer Yes were (43.33%), regarding animals around house most of participants answer No were (51.67%) while answer Yes were (47.33%) , regarding the nationality the majority of participant Saudi were (88.33%) followed by non-Saudi were (11.67%)

Table 2 Distribution of Clinical features of Cutaneous Leishmaniasis active skin lesions.

Lesion	**N**	**%**
Type		
Nodular	29	48.33
Ulcerative	20	33.33
Unknown	11	18.33
Ulcer		
Wet	25	41.67
Dry	35	58.33
Duration		
<6 months	36	60.00
6-12 months	7	11.67
>12 months	17	28.33
Location		
Face	10	16.67
Upper limbs	7	11.67
Lower limbs	43	71.67
Number		
Single	24	40.00
Double	14	23.33
Multiple	22	36.67
Surface area		
1-5 cm	8	13.33
5-10 cm	29	48.33
>10 cm	23	38.33

This table 2 distribution of Clinical features of Cutaneous Leishmaniasis active skin lesions shows regarding the type the majority of participants approximately (48.33%) were nodular while ulcerative were (33.33%) followed by unknown were (18.33%), regarding ulcer, more than half of participant (58.33%) were dry followed by wet were (41.67%), regarding duration the majority of participant <6 months were (60.00%) followed by >12 months were (28.33%) while 6-12 months were (11.67%) , regarding location the majority of participant (71.67%) were lower limbs followed by face were (16.67%) while upper limbs were (11.67%), regarding number most of participants single were (40.0%) followed by multiple were (36.67%) while

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double were (23.33%), regarding the surface area the majority of participant 5-10 cm were (48.33%) followed by >10cm were (38.33%) while 1-5cm were (13.33%) .

Table 3 Distribution of lesions on different body parts of patients from Makah .

Site		Positive smears		Negative smears		Total number	
		No	%	No	%	No	%
Face		19	76.00	6	24.00	25	41.67
Arms		12	54.55	10	45.45	22	36.67
Legs		8	61.54	5	38.46	13	21.67
Total		39	65.00	21	35.00	60	100.00
Chi-square	**X^2**	2.455					
	P-value	0.293					

This table 3 distribution of lesions different body parts of patients shows the lesion distribution is concerned majority of participant have positive smears in face, legs and arms had (76.0%, 61.54% and 54.55%) lesions, respectively while total were (65.0%) , regarding the lesion negative smears distribution the majority of participant have in arms, legs and face had (45.45%, 38.46% and 24.0%) lesions, respectively while total were (35.0%) while no significant relation were P=0.293 while X^2 2.455 .

Figure (1): Distribution of lesions on different body parts of patients from Makah

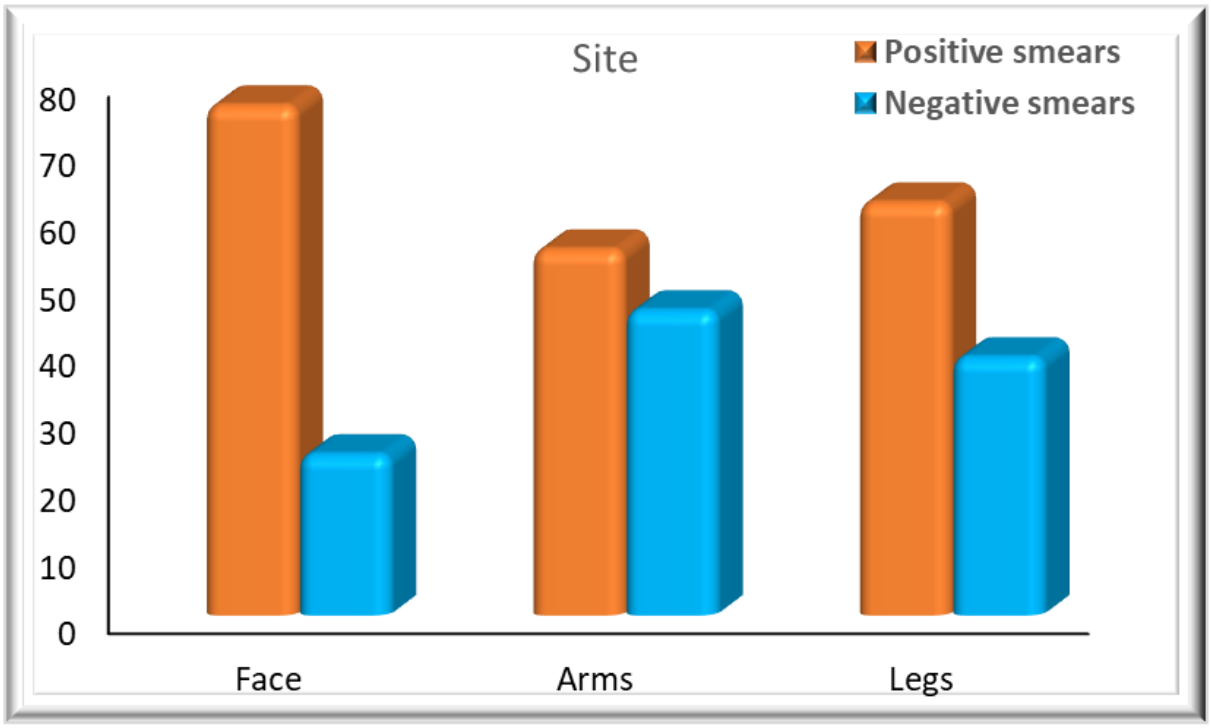

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Table 4: Distribution of the liver enzymes (AST & ALT), creatinine and urea in 20 cutaneous leishmaniasis patients treated with fluconazole .

Fluconazole 3(200 mg/d)	After 15 days	After 60 days	Difference		Paired T-test	
	Mean ± SD	Mean ± SD	Mean	SD	t	P-value
AST (IU/L) (0-45 IU/L)	27.55 ± 3.03	45.05 ± 2.84	16.87	5.65	23.12822	<0.001*
ALT (IU/L) (3-60 IU/L)	19.28 ± 1.87	65.25 ± 3.19	43.57	2.112	159.7972	<0.001*
Creatinine (72.0-126 µmoles/L)	81.721 ± 2.97	83.94 ± 2.84	2.01	8.15	1.910355	0.115
Urea (3.0-6.0 µmoles/L)	2.115 ± 0.53	3.157 ± 0.4298	1.089	0.123	68.58014	<0.001*

Regarding the distribution of the liver enzymes (AST & ALT), creatinine and urea in 20 cutaneous leishmaniasis patients treated with Fluconazole 3(200 mg/d) values of these enzymes remained at higher side but within the normal range on 15th and 60th days of medications (Fig. 2 & 3), regarding the AST (IU/L) (0-45 IU/L) after 15 days and 60 days recipictvly Mean ±SD (27.55±3.03 and 45.05 ±2.84) while difference in Mean and SD (16.87 , 5.65) while a significant relation were P=0.001 while t= 23.12822, regarding the ALT (IU/L) (3-60 IU/L) after 15 days and 60 days recipictvly Mean ±SD (19.28 ± 1.87and 65.25 ± 3.19) while difference in Mean and SD (43.57 , 2.112) while a significant relation were P=0.001 while t= 159.7972, regarding the Creatinine (72.0-126 µmoles/L**)** after 15 days and 60 days recipictvly Mean ±SD (81.721 ± 2.97and 83.94 ± 2.84) while difference in Mean and SD (2.01 , 8.15) while no significant relation were P=0.115 while t= 1.910355, regarding the Urea (3.0-6.0 µmoles/L) after 15 days and 60 days recipictvly Mean ±SD (2.115 ± 0.53and 3.157± 0.4298) while difference in Mean and SD (1.089 , 0.123) while a significant relation were P=0.001 while t= 68.58014

Figure (2) : Distribution of the liver enzymes (AST), creatinine and urea in 20 cutaneous leishmaniasis patients treated with fluconazole after 15 , 60 days

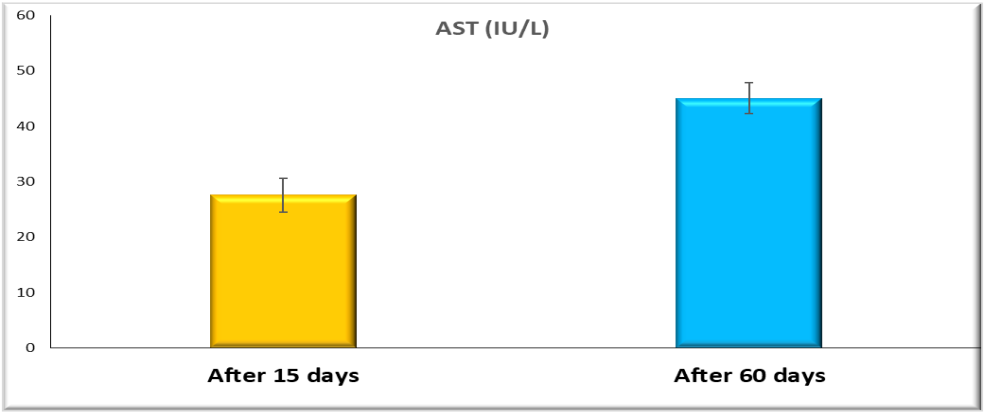

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Figure (3) : Distribution of the liver enzymes (ALT), creatinine and urea in 20 cutaneous leishmaniasis patients treated with fluconazole after 15, 60 days

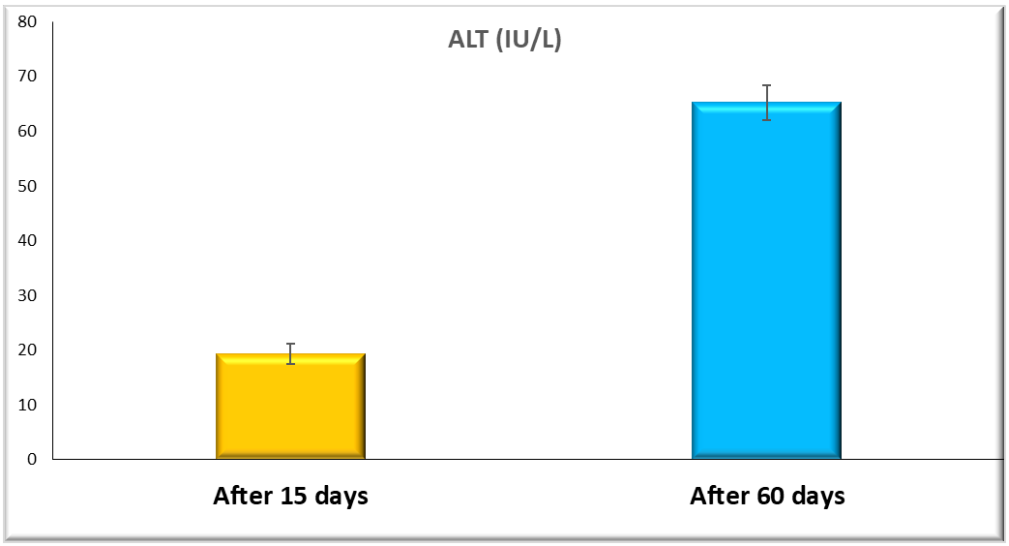

Figure (4) : Distribution of the liver enzymes (ALT), creatinine in 20 cutaneous leishmaniasis patients treated with fluconazole after 15, 60 days

Figure (5) : Distribution of the liver enzymes (ALT) urea in 20 cutaneous leishmaniasis patients treated with fluconazole after 15, 60 days

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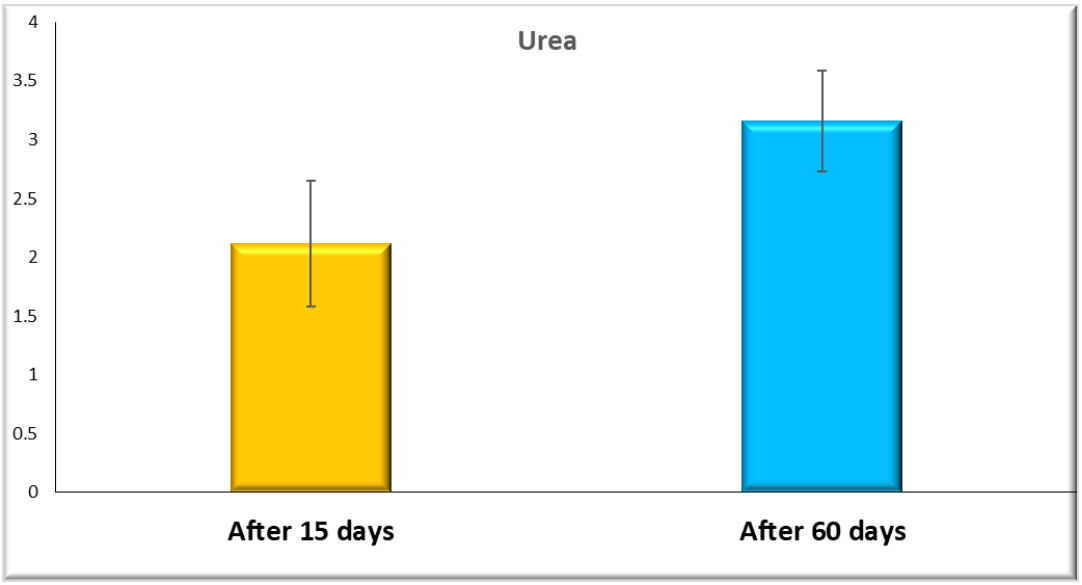

Discussion

During this relatively-short study period, 60 patients with active leishmanial skin lesions were identified in the study's setting. Factors like the increasing urbanization close to the nearby endemic foci, the growing population's size and the frequent population's movement could be explanations. Moreover, the progress made in disease's diagnosis and the increase in population's awareness towards the value of early treatment may be additional explanations. Taken together, it was clear that CL in the study setting is more frequent than perceived in the literature and mandate further attention from the health authorities. CL cases were reported all the year around, but most of the cases were reported in the winter, in agreement with previous Saudi studies [31]. In our study shows distribution of the Socio-demographic characteristics, the majority of participants approximately (30.0%) were aged from 31-40 years, regarding sex, more than half of participant (53.33%) were male , regarding the location of lesions the majority of participant head, face, and neck were (45.0%), regarding number of lesions most of participants from 3–4 were (40.0%) , regarding the residence the majority of participant urban were (81.0%), regarding animals around house answer Yes were (47.33%) (See table 1)

Conversely, in a study, carried out in southeastern Tunisia, most of the cases were recorded in the summer [15]. The local climate and its effects on the host-vector activities could explain seasonality variations among different studies [16]. All CL lesions were confined to the skin with no mucosal tissue involvement or nodular dissemination noticed in all cases, consistent with previous studies [32] and inconsistent with others [20]. Also in another study, the microscopic examination of stained smear prepared from lesion's scraping displayed sensitivity of 74%, higher than that previously reported. Sensitivities of 42% -70% have been reported in earlier studies [33]. Factors like the therapeutic regimen, the causative leishmania species, the lesion's severity and duration, and the patient's immune and health status, all can explain the variations of the drug efficacy displayed among studies [29]. Before pentostam treatment, highly significant levels of IFN-γ and NO were exhibited in healing than non-healing patients groups, in agreement with an earlier study [30]. Conversely, Taheri et al. [31] Similar our study distribution of Clinical features of Cutaneous Leishmaniasis active skin lesions

shows regarding the type the majority of participants approximately (48.33%) were nodular while ulcerative were (33.33%), regarding ulcer, more than half of participant (58.33%) were dry followed by wet were (41.67%), regarding duration the majority of participant <6 months were (60.00%) , regarding location the majority of participant (71.67%) were lower limbs , regarding number most of participants single were (40.0%), regarding the surface area the majority of participant 5-10 cm were (48.33%) .(See table 2)

These results are in contrast to the findings from a study regarding distribution of lesions different body parts of patients shows the lesion distribution is concerned majority of participant have positive smears in face, legs and arms had (76.0%, 61.54% and 54.55%) lesions, respectively while total were (65.0%) , regarding the lesion negative smears distribution the majority of participant have in arms, legs and face had (45.45%, 38.46% and 24.0%) lesions, respectively while total were (35.0%) while no significant relation were P=0.293 while X2 2.455 (See table 3). Similar we have noticed lack of awareness among people regarding transmission and prevention of disease. Similar lack of awareness had also been reported among patients from Al-Hassa [34].

We observed slightly raised figures for AST and ALT activities, 63.83±3.71, 57.42±2.84 and 77.61±3.35, 68.8±1.72 IU/L after 45 days of treatment with fluconazole and itraconazole, respectively, which regained their normal physiological values after 15 days of termination of medications. Almost similar efficacy was observed with fluconazole and itraconazole in Kuwait, India and Saudi Arabia [29]. Similar reversible rise with these drugs was also indicated in a review of Khan et al. [35]. Since liver is major site of drug metabolism, increased level of AST and ALT in blood might be due to the effect of fluconazole and itraconazole which were administered for a prolonged duration to treat skin lesions and hence might have damaged the liver and leakage of enzyme had occurred which quickly recovered after the termination of treatment. Creatinine was also slightly increased in patients during the terminal phase of treatment with both fluconazole and itraconazole. Similar our study the distribution of the liver enzymes (AST & ALT), creatinine and urea in 20 cutaneous leishmaniasis patients treated with Fluconazole 3(200 mg/d) values of these enzymes remained at higher side but within the normal range on 15th and 60th days of medications (Fig. 2 & 3,4 &5), regarding the ALT (IU/L) (3-60 IU/L) after 15 days and 60 days recipictvly Mean ±SD (19.28 ± 1.87and 65.25 ± 3.19) while difference in Mean and SD (43.57 , 2.112) while a significant relation were P=0.001 while t= 159.7972, regarding the Creatinine (72.0-126 μmoles/L) after 15 days and 60 days recipictvly Mean ±SD (81.721 ± 2.97and 83.94 (2.84 ±while difference in Mean and SD (2.01 , 8.15) while no significant relation were P=0.115 while t= 1.910355 (See table 4)

Conclusion

KSA is still considered endemic for CL; more efforts and integrated approaches are needed to combat this disease. To handle the potential risk factors, it is advisable for the urbanization process and construction of new buildings to be preceded by some ecological and biological assessments to avoid as much as possible the invasion of disease natural habitats and to apply some control activities if needed. However, vector control activities and health education on use of personal protection measures should be carried out regularly during Hajj pilgrimage to prevent many vector borne diseases, including CL. The disease is endemic in many parts of the

country; in some regions neither the causative species nor the incriminated sand fly was identified. Therefore, scientific research should be encouraged to address all aspects of the disease. Actually, identification of the involved parasite species has a major role in decision making concerning management of patients.

Reference

[1] de Vries, H. J., & Schallig, H. D. (2022). Cutaneous leishmaniasis: a 2022 updated narrative review into diagnosis and management developments. *American Journal of Clinical Dermatology*, *23*(6), 823-840.

[2] Rasheed, Z., Ahmed, A. A., Salem, T., Al-Dhubaibi, M. S., Al Robaee, A. A., & Alzolibani, A. A. (2019). Prevalence of Leishmania species among patients with cutaneous leishmaniasis in Qassim province of Saudi Arabia. *BMC public health*, *19*(1), 1-8.

[3] Lozano, Y. Y., Giraldo, S. E., Zapata, A. C., Escobar, J. E., & Sánchez, R. M. (2023). Medicinal plants with antileishmanial activity on parasites responsible for new-world cutaneous leishmaniasis. A systematic review 2018-2022. *Journal of Pharmacy & Pharmacognosy Research*, *11*(6), 975-1001.

[4] Pal, M., Ejeta, I., Girma, A., Dave, K., & Dave, P. (2022). Etiology, clinical spectrum, epidemiology, diagnosis, public health significance and control of Leishmaniasis: A comprehensive review. *Acta Scientific MICROBIOLOGY (ISSN: 2581-3226)*, *5*(5).

[5] Kumosani, T. A., Al-Bogami, T. J., Barbour, E. K., Alshehri, S. H., Yaghmoor, S. S., Alshareef, N. A., ... & Moselhy, S. S. (2022). Leishmaniasis prevalence, awareness and control in Saudi Arabia. *African Health Sciences*, *22*(3), 640-647.

[6] Benallal, K. E., Garni, R., Harrat, Z., Volf, P., & Dvorak, V. (2022). Phlebotomine sand flies (Diptera: Psychodidae) of the Maghreb region: A systematic review of distribution, morphology, and role in the transmission of the pathogens. *PLoS Neglected Tropical Diseases*, *16*(1), e0009952.

[7] Cecílio, P., Cordeiro-da-Silva, A., & Oliveira, F. (2022). Sand flies: Basic information on the vectors of leishmaniasis and their interactions with Leishmania parasites. *Communications biology*, *5*(1), 305.

[8] Bennis, I., De Brouwere, V., Belrhiti, Z., Sahibi, H., & Boelaert, M. (2018). Psychosocial burden of localised cutaneous Leishmaniasis: a scoping review. *BMC public health*, *18*, 1-12..

[9] Reimão, J. Q., Coser, E. M., Lee, M. R., & Coelho, A. C. (2020). Laboratory diagnosis of cutaneous and visceral leishmaniasis: current and future methods. *Microorganisms*, *8*(11), 1632.

[10] Gow, I., Smith, N. C., Stark, D., & Ellis, J. (2022). Laboratory diagnostics for human Leishmania infections: a polymerase chain reaction-focussed review of detection and identification methods. *Parasites & Vectors*, *15*(1), 412.

[11] Sampaio, R. N. R. (2023). Pharmacotherapy in leishmaniasis: Old, new treatments, their impacts and expert opinion. *Expert Opinion on Pharmacotherapy*, *24*(2), 153-158.

[12] Dinc, R. (2022). New developments in the treatment of cutaneous leishmaniasis. *Asian Pacific Journal of Tropical Medicine*, *15*(5), 196-205.

[13] Chakravarty, J., & Sundar, S. (2019). Current and emerging medications for the treatment of leishmaniasis. *Expert opinion on pharmacotherapy*, *20*(10), 1251-1265.

[14] Mazire, P., Agarwal, V., & Roy, A. (2022). Road-map of pre-clinical treatment for Visceral Leishmaniasis. *Drug Development Research*, *83*(2), 317-327.

[15] Registre, C., Soares, R. D., Rubio, K. T., Santos, O. D., & Carneiro, S. P. (2023). A Systematic Review of Drug-Carrying Nanosystems Used in the Treatment of Leishmaniasis. *ACS Infectious Diseases*, *9*(3), 423-449.

[16] Madusanka, R. K., Silva, H., & Karunaweera, N. D. (2022). Treatment of cutaneous leishmaniasis and insights into species-specific responses: a narrative review. *Infectious diseases and therapy*, *11*(2), 695-711.

[17] Wijnant, G. J., Dumetz, F., Dirkx, L., Bulté, D., Cuypers, B., Van Bocxlaer, K., & Hendrickx, S. (2022). Tackling drug resistance and other causes of treatment failure in leishmaniasis. *Frontiers in Tropical Diseases*, *3*, 837460.

[18] Wajihullah, K. H. A. N., & Zakai, H. A. (2014). Epidemiology, pathology and treatment of cutaneous leishmaniasis in Taif region of Saudi Arabia. *Iranian journal of parasitology*, *9*(3), 365.

[19] Abbasi, E., & Saeedi, S. (2022). A perspective on human leishmaniasis and new methods with therapeutic strategies for prevention, diagnosis, and treatment.

[20] Lotfy, W. M., & Alsaqabi, S. M. (2016). Climate change and epidemiology of human parasitoses in Saudi Arabia: A review. *Journal of Coastal Life Medicine*, *4*(7), 580-588.

[21] Shalaby, I., Gherbawy, Y., Jamjoom, M., & Banaja, A. E. (2011). Genotypic characterization of cutaneous leishmaniasis at al Baha and Al Qasim provinces (Saudi Arabia). *Vector-Borne and Zoonotic Diseases*, *11*(7), 807-813.

[22] Selim, A., Alanazi, A. D., Sazmand, A., & Otranto, D. (2021). Seroprevalence and associated risk factors for vector-borne pathogens in dogs from Egypt. *Parasites & vectors*, *14*(1), 1-11.

[23] El-Beshbishy, H. A., Al-Ali, K. H., & El-Badry, A. A. (2013). Molecular characterization of Leishmania infection in sand flies from Al-madinah Al-munawarah province, western Saudi Arabia. *Experimental parasitology*, *134*(2), 211-215.

[24] Alanazi, A. D., Puschendorf, R., Alyousif, M. S., Al-Khalifa, M. S., Alharbi, S. A., Al-Shehri, Z. S., ... & ALRAEY, Y. A. (2019). Molecular detection of Leishmania spp. in skin and blood of stray dogs from endemic areas of cutaneous leishmaniasis in Saudi Arabia. *Iranian Journal of Parasitology*, *14*(2), 231.

[25] Bousslimi, N., Aoun, K., Ben-Abda, I., Ben-Alaya-Bouafif, N., Raouane, M., & Bouratbine, A. (2010). Epidemiologic and clinical features of cutaneous leishmaniasis in southeastern Tunisia. *The American journal of tropical medicine and hygiene*, *83*(5), 1034.

[26] Abuzaid, A. A., Abdoon, A. M., Aldahan, M. A., Alzahrani, A. G., Alhakeem, R. F., Asiri, A. M., ... & Memish, Z. A. (2017). Cutaneous leishmaniasis in Saudi Arabia: a comprehensive overview. *Vector-Borne and Zoonotic Diseases*, *17*(10), 673-684.

[27] Zakai, H. A. (2014). Cutaneous leishmaniasis in Saudi Arabia: current status. *Journal of Advanced Laboratory Research in Biology*, *5*(2).

[28] Siebert, C., Rosenthal, E., Möller, P., Rödiger, T., & Meiler, M. (2012). The hydrochemical identification of groundwater flowing to the Bet She'an-Harod multiaquifer system (Lower Jordan Valley) by rare earth elements, yttrium, stable isotopes (H, O) and Tritium. *Applied Geochemistry*, *27*(3), 703-714.

[29] Amin, T. T., Al-Mohammed, H. I., Kaliyadan, F., & Mohammed, B. S. (2013). Cutaneous leishmaniasis in Al Hassa, Saudi Arabia: epidemiological trends from 2000 to 2010. *Asian Pacific journal of tropical medicine*, *6*(8), 667-672.

[30] Faraj, C., Ouahabi, S., Adlaoui, E. B., El Elkohli, M., Lakraa, L., El Rhazi, M., & Ameur, B. (2012). Insecticide susceptibility status of Phlebotomus (Paraphlebotomus) sergenti and Phlebotomus (Phlebotomus) papatasi in endemic foci of cutaneous leishmaniasis in Morocco. *Parasites & vectors*, *5*, 1-6.

[31] Knight, C. A., Harris, D. R., Alshammari, S. O., Gugssa, A., Young, T., & Lee, C. M. (2023). Leishmaniasis: Recent epidemiological studies in the Middle East. *Frontiers in Microbiology*, *13*, 1052478.

[32] Al-Koleeby, Z., El Aboudi, A., Van Bortel, W., Cloots, K., Benkirane, R., Faraj, C., & Talbi, F. Z. (2022). Ecological Survey of the Peridomestic Sand Flies of an Endemic Focus of Zoonotic Cutaneous Leishmaniasis in the South-East of Morocco. *The Scientific World Journal*, *2022*.

[33] Rocha, R., Pereira, A., & Maia, C. (2022). Non-Endemic Leishmaniases Reported Globally in Humans between 2000 and 2021—A Comprehensive Review. *Pathogens*, *11*(8), 921.

[34] Soleimani, H., Jafari, R., Veysi, A., Zahraei-Ramazani, A. R., Rassi, Y., Mirhendi, H., ... & Akhavan, A. A. (2022). An outbreak of cutaneous leishmaniasis due to Leishmania major in an endemic focus in central Iran. *Journal of Parasitic Diseases*, *46*(2), 502-510.

[35] Khan, K., Sajjad, M., Wahid, S., Gul, M., Khan, L., Ullah, H., ... & Shah, S. U. (2022). Bionomics of the unexplored sand flies fauna of District Mohmand, Khyber Pakhtunkhwa, Pakistan: assessing risk factors associated with cutaneous leishmaniasis. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, *116*(9), 832-844.