An-Najah National Univer	SILV
--------------------------	------

Faculty of Graduate Studies

Epidemiology of Cutaneous Leishmaniasis in the Northern West Bank, Palestine

 $\mathbf{B}\mathbf{y}$

Wesam Sbehat

Supervisor

Dr. Ayman Hussein

This Thesis is Submitted in Partial Fulfillments of the Requirements for the Degree of Master in Public Health, Faculty of Graduate Studies, An-Najah National University, Nablus, Palestine.

Epidemiology of Cutaneous Leishmaniasis in the Northern West Bank, Palestine

By

Wesam Sbehat

This thesis was defended successfully on 27/9/2012 and approved by:

1. Dr. Ayman Hussein (Supervisor) 2. Dr. As'ad Ramlawi (External Examiner) 3. Dr. Walid Basha (Internal Examiner)

Dedication

For

My family, who offered me unconditional love and support throughout the course of this thesis. To my friends and colleagues.

Acknowledgment

Thanks and gratitude to my supervisor, Dr. Ayman Hussein for his guidance, encouragement and help through this study.

My special thanks to all those who helped me in my study, deepest respect and appreciation to D.G of primary health care and public health in the Palestinian ministry of health DR. .Asad Ramlawi and all of my friends and colleagues ,Directors of health issues in the primary health care department and the preventive medicine department of all districts , for their cooperation . Special thanks to my dear colleague head of vectors environmental department Samir Sawalha . My special and deepest thanks, respect and appreciation to my dear mother, father, sisters and my brothers for their patience and encouragement Lastly, I offer my regards and blessings to all of those who supported me in any respect during the completion of the thesis. and everyone wanted me to succeed progress and develop and shared me with their emotions.

٧ الاقرار

انا الموقع ادناه مقدم الرسالة التي يحمل العنوان

Epidemiology of cutaneous leishmaniasis in the northern west bank ,Palestine

وبائية داء الليشمانيا الجلدية في شمال الضفة الغربية فلسطين

اقر بأن ما اشتملت عليه هذه الرسالة إنما هي نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وإن هذه الرسالة ككل، أو أي جزء منها لم يقدم من قبل لنيل أية درجة علمية أو بحث علمي أو بحثي لدى أية مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: : اسم الطالب

Signature : التوقيع :

Date : التاريخ

Table of Contents

No.	Subject	Page
	Dedication	iii
	Acknowledgments	iv
	Declaration	V
	List of tables	viii
	List of figures	ix
	Abbreviations	X
	Abstract	xi
	CHAPTER ONE	1
	Introduction	2
1.1	Background	2
1.1.1	Parasite	2
1.1.2	Life cycle	3
1.1.3	Clinical forms of Leishmaniasis	4
1.1.4	Transmission	7
1.1.5	Public Health Surveillance	11
1.1.6	Clinical diagnosis and identification	12
1.1.7	Treatment	13
1.2	Significance of the study	13
	CHAPTER TWO	15
2	Literature Review	16
2.1	Epidemiology and Environmental factors	16
2.2	Incidence of leishmaniasis in the World and in the	16
	Eastern Mediterranean region	
2.3	Leishmaniasis in Palestine	18
	CHAPTER THREE	21
3.1	Patients and study area	22
3.2	Design of the study	23
3.3	Sample collection	24
	CHAPTER FOUR	26
4.1	Distribution of study participants	27
4.2	Year of infection and districts	28
4.3	Demographic and epidemiologic characteristics of CL	29
	patients in Northern West Bank, Palestine (2000-2010)	
4.4	Place of residence	29
4.5	profession	30
4.6	Site of infection	31
4.7	Number of nodules	32

4.8	Type of animals living in contact with patients with CL	33
4.9	Existing of dogs and rats around the area of patients	34
	with CL	
4.10	Environmental hazards around where people live	36
4.11	Presence of screens on windows	37
4.12	Use of insecticides inside homes of study participants	38
4.13	Use of Namosiya by participants	39
4.14	Geography of houses and presences of caves around	40
	patients residences	
CHAPTER FIVE		42
5.1	Discussion	43
5.2	Conclusion	47
5.3	Recommendations	48
	D - f	49
	Referrences	49
	Appendices	62

List of Tables

No.	Subject	Page
1	Age categories of study participants	27
2	Number of patients with cutaneous leishmanisis distributed into districs of North west Bank	28
3	Distribution of domestic animals near patients with CL.	33

List of Figures

No.	Subject	Page
1	Forms of the parasite <i>Leishmania</i> : (A) and promastigote (B)	3
2	Life cycle of <i>Leishmania</i> parasite	4
3	Picture showing nodules on face of patient with CL	5
4	CL Patients with ulcer on the face.	6
5	Sand fly vector of Leishmania spp.	8
6	Fat sand rat	9
7	Gerbil animal	9
8	Hyrax animal	11
9	Map of the Palestinian governorates according to Palestinian classification.	23
10	Distribution of study samples by residence (Total number of study samples is 1150).	27
11	Distribution of sex of patients with cutaneous leishmaniasis	29
12	Place of living of patients with CL.	30
13	The profession of patients with CL in North West Bank	31
14	Site of infections of CL as found on study participants.	32
15	Distribution of nodules among patients with CL in North of west Bank	33
16	Existing of rats (A) or holes for rats (B) where patients with CL live.	35
17	Existence of dogs around the patients with CL houses (numbers in the X-axis represents number of dogs).	36
18	Accumulation of waste around the area where patients with CL are living.	37
19	Presence of window screens (nets) in the houses of patients with CL	38
20	Use of insecticides insides houses of patients with CL.	39
21	Use of net covers (namosiya) by patients of CL in their beds.	40
22	Distribution of patient's houses.	41
23	Presence of caves and cracks near the residence of patients with CL.	41

Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
CDC	Centre o Disease Control and Prevention
CL	Cutaneous Leishmaniasis
DDT	Dichlorodiphenyltrichloroethane
EMR	Estern Mediterian Region
HIV	Human Immunodeficiency Virus
IRB	Internal Review Board
MCL	Mucocutaneous Leishmaniasis
MOH	Ministry of Health
NW	New World
OW	Old World
PCR	Polymerase Chain Reaction
SPSS	Statistical Package for the Social Sciences
VL	Visceral leishmaniasis
WHO	World Health Organization

Epidemiology of cutaneous leishmaniasis in the northern west bank, Palestine

By Wesam Sbehat Supervisor Dr. Ayman Hussein

Abstract

BACKGROUND: Leishmaniasis has been an antique public health problem in south -West Asia and the Arab world reported from time immemorial as the pharaohs ruled in Egypt and Assyrians in Mesopotamia. The disease is caused by the genus Leishmania. There are several species of this parasite that cause leishmaniasis where three forms are confirmed: cutaneous (CL), mucco-cutaneous (MCL), and visceral (VL) leishmaniasis. North of Palestine is the centre of a region where simple CL is hyperendemic. Leishmania parasite is transmitted by the sand fly vector supported by a wide range of reservoirs distributed on all inhabited continents. In Palestine, two forms of leishmaniasis exist. One is the CL caused by L. major or L. tropica and the other is visceral caused by L. infantum. Leishmaniasis in general is reported in all Palestinian districts except Gaza strip with an official incidence rate in the West Bank of more than 10 per 100,000 in 2003. AIM: The epidemiology of CL in Palestine and neighbouring countries appears to be undergoing a transition. From our observation as worker in MOH clinic for infectious diseases, we noticed rise in number of patients with CL in the area of north West Bank. Therefore, this study was designed to study the incidence of CL over 10 years period as well as studying the ecological, epidemiological and social factors that might lead to this rise. Methodology: This study is retrospective cross-sectional study. 1150 files of patients were reviewed in order to fill a questionnaire designed by the authors. The questionnaire includes demographic, clinical, diagnostic, and epidemiological questions. Age, residence, sex and personal information as well as information about domestic and wild animal living around patients were collected. Other information about houses and protective measures taken by respondents to avoid bite of the sand fly vector were also seeked. **RESULTS**: The most striking results found in this study was that the study confirms that the area understudy is hyperendemic with CL. Tubas and Jenin districts were found to have more incidence by at least 5-10 than other districts in this study. No difference was found between male and female in infection with CL. However, children found to be the most affected age group. Site of infection among patients showed that limbs and legs are predominantly affected. Rat and dogs were reported by patients around their houses. Those animals are known to act as reservoirs for Sand fly vector. More than 70% of CL patients were found resident of suburban areas, although patients from different geographical sites were found.

Chapter One

Introduction

Introduction

1.1. Background

1.1.1. Parasite

Leishmania parasite is a protozoa belonging to the order Kinetoplastida and the family of Trypanosomatidae. The genus Leishmania includes more than 20 species. The parasite exists in two morphological forms: the non-flagellated amastigote (3-5 mm in diameter) living intracellular in macrophages of the mammalian host (Figure 1A), and the flagellated promastigote, living extracellular in the intestinal tract of the sandfly-vector (figure 1B). In the macrophages the amastigotes are able to survive and multiply within the acidic phagolysosomes of the host cells (reviewed by Alexander et al., 1999). After multiplication in the host cell the amastigotes are released. Subsequently other macrophages are infected and the infection spreads (reviewed by Peters et al., 1990; Rittig and Bogdan, 2000). The parasite contains two prominent organelles, the nucleus and the kinetoplast. The kinetoplast is found in all protozoa of the order kinetoplastidae (eg. Leishmania, Trypanosoma, Crithidia).

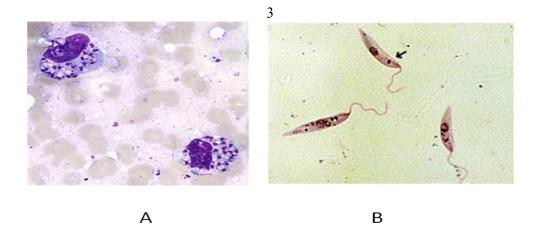


Figure 1. Forms of the parasite *Leishmania*: (A) and promastigote (B).

1.1.2 Life cycle:

The transmission cycle is maintained between the vector and the reservoir. Depending on the species of *Leishmania*, the transmission is either zoonotic or anthroponotic, involving either animals or humans as reservoir (Figure 2). The parasite is transmitted by the bite of female sandflies of the genus *Phlebotomus* and *Lutzomyia*. During the blood meal *Leishmania* infected macrophages are ingested by the vector. In the gut of the sandfly the intracellular amastigotes develop into flagellated promastigotes at an ambient temperature of 24-28°C. During another blood meal the mature promastigotes are inoculated into a mammalian host. Macrophages ingest the parasites, which then transform into the amastigote form.

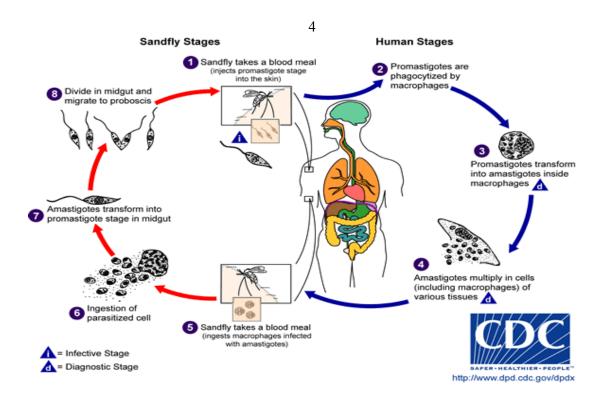


Figure 2. Life cycle of *Leishmania* parasite

1.1.3. Clinical forms of leishmaniasis.

In most patients, the skin lesion begins as a small erythematous papule about 2 to 6 weeks after inoculation (figure 3). Over the following month the papule slowly enlarges, and a crust develops in its centre. With time, the crust falls away, exposing a shallow ulcer (see figure 4). (Klaus and Frankenburg, 1999; AL Jawabreh et al., 2004).

Figure 3. Picture showing nodules on face of patient with CL(Klaus and Frankenburg, 1999; AL Jawabreh *et al.*, 2004).

If no treatment is given, the nodules ulcer remains stable for 6 to 12 months before undergoing spontaneous resolution. Usually a shallow depressed scar is left behind. CL caused by L. tropica and L. major are indistinguishable on clinical bases as both erupt in the same way, the size of the lesion ranging from a few millimeters to 4 centimeter or more. The site and number of lesions(s) are an indication of the type of cutaneous (CL). L. major usually presents as multiple lesions (\geq 3) and L.tropica is more often on the nose (Klaus and Frankenburg, 1999; AL Jawabreh et al., 2004).

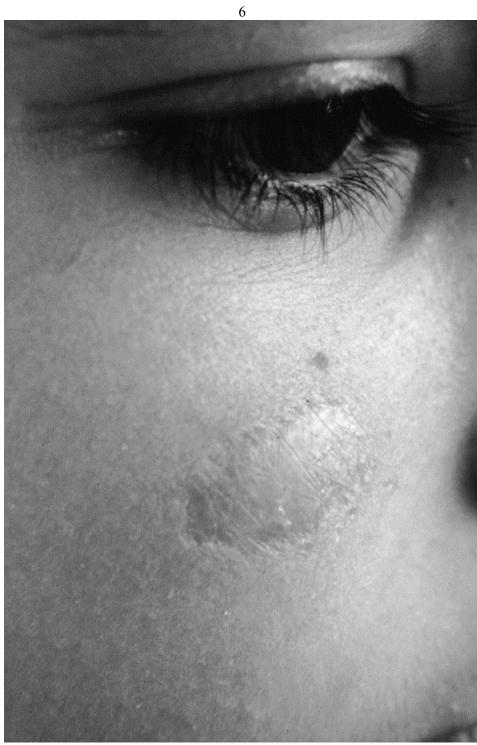


Figure 4. CL Patients with ulcer on the face. (Al-Jawabreh et al., 2004).

The preferred sites for *L. major* are cheeks, arms and legs which account for more than 70% of the cases, while the preferred sites for *L. tropica* are cheeks and arms forming over 50% (**Al-Jawabreh** *et al.*, 2004). Abnormal manifestations for *L. major* are the enlargement of regional lymph nodes which is found in about 10% of patients. At times, the infection spreads deeply into subcutaneous tissue and muscle (**Al-Gindan** *et al.*, 1989; **Vardy** *et al.*, 1993). Hyperesthesia or anesthesia around the lesion was reported (**Satti** *et al.*, 1989).

The three distinct forms, cutaneous Leishmaniasis (CL), visceral (VL) and mucocutaneous leishmaniasis (MCL) are classically caused by a spectrum of different *Leishmania* species. Even though there is a clear correlation between the causative species and the clinical presentation, many variations are seen. Depending on the specific characteristics of species/strains and also on the immunocompetence of the host the clinical manifestation may vary to a great extent. Species causing typically CL may visceralize and visceral species may show dermatotropism. In many endemic areas of the world a few *Leishmania* species are prevalent simultaneously so that a species specific diagnosis can not rely on clinical findings alone. Species specific diagnosis is necessary for adequate treatment. (Schlein *et al.*, 1982; 1984).

1.1.4. Transmission:

The presence of leishmaniasis depends on a variety of ecological and biological factors. Since the various *Leishmania* species depend as much on

specific reservoir as on specific vector species, a *Leishmania* focus can only exist if suitable ecological conditions are present for both the host animal species and the sand fly species (fig. 5).



Figure 5. Sand fly vector of Leishmania spp.

CL occurs either as a zoonotic or an anthroponotic infection. Zoonotic CL is caused by *L.major*, with rodents serving as the reservoir. These rodents live usually in colonies and are commonly found in vast uninhabited areas. The rodent burrows provide excellent breeding places for the sandflies. Through the coexistence of rodents and sandflies in the same habitat the natural transmission cycle of *L.major* is maintained. In zoonotic leishmaniasis humans are only accidental hosts. New endemic foci of CL can emerge when developmental changes take place (eg. building, agriculture). In the Middle East and North Africa the fat sand rat (*Psammomys obesus*) is the main reservoir (Figure 6). Also jirds (*Meriones* sp.) (figure 7) were found to host the parasite (**Schlein** *et al.*, **1982**; **1984**).



Figure 6. Fat sand rat.



Figure 7. Gerbil animal.

In Central Asia, Iran and Afghanistan the great gerbil (*Rhombomys opimus*) was identified as being the reservoir of *L.major* (**Strelkova**, **1996**; **Yaghoobi-Ershadi and Javadian**, **1996**). This gerbil species also hosts nonpathogenic species of *Leishmania* (*L.gerbilli* and *L.turanica*). *L.major* is transmitted predominantly by sandflies of the species *Ph.papatasi*. Anthroponotic CL has been attributed to *L.tropica*. Major urban centers of the Middle East (Aleppo, Damascus, Baghdad, Tashkent, Teheran and Kabul) were known to be highly endemic for *L.tropica*. Humans are the only known reservoir. The infections were so numerous as to maintain the

transmission cycle. In recent years it became increasingly obvious that the classical transmission pattern of *L.tropica* infections has changed. Epidemics in densely populated areas became less common. A shift from an urban to a rural distribution took place. In some of the mentioned Middle Eastern cities, CL has been quite efficiently eradicated by systematic and repeated spraying of houses with insecticides and also as a result of spraying within anti-malaria campaigns. In the past decade the outskirts of cities and villages have been affected predominantly, and infections have occurred more sporadically. These characteristics suggest the existence of an animal reservoir and a zoonotic transmission of L. tropica. Until today the animal reservoir of L. tropica has not been identified, but several animal species are suspected to function as reservoir. L. tropica has been isolated from hyrax (*Procavia* ssp.) in Kenya (**Marlet** et al., 2003), from dogs in Morocco (Dereure, 1991) and from rat x (Aljeboori and Evans, 1980). Hyraxes are the proven reservoir of L.aethiopica in Ethiopia (Ashford et al., 1973; Bray et al., 1973). In Jordan hyraxes (figure 8) are abundant in endemic areas of L. tropica and are therefore suspected to be the reservoir (Saliba et al., 1997). This has been discussed also by Ashford, (2000). L. tropica is predominantly transmitted by sandflies of the species *Ph* . *sergenti*.



Figure 8. Hyrax animal.

1.1.5. Public Health Surveillance:

Leishmaniasis is a reportable infection in Palestine (Ministry of Health, 2004) and all neighboring countries like Jordan, Syria and Saudi Arabia. Ministries of Health collect data for various reasons like therapeutic and control strategies. Despite the law mandate, underreporting is still believed to prevail partly due to passive surveillance, including only cases coming from clinics and hospitals. Already before 1994 when the health authority was in the hands of the Israeli military rule, there were attempts to improve the reporting system in Palestine (Awad et al., 2001). After 1994, the Palestinian Ministry of health continued the surveillance activity but suffered some disturbances between 2001 and 2005 due to the political turmoil in the area. The current situation depends on passive collection of data from health care providers in all Palestinian districts by the preventive medicine department in the Ministry of Health and presenting them either on the official website or distributing hardcopies to health stake-holders in the regions. The aim of surveillance is to control and prevent diseases, improve epidemiological knowledge and assist policy making. The tripod

of this activity is the laboratory, physicians/nurses and epidemiologist/statistician.

1.1.6. Clinical diagnosis and identification:

The conventional methods of clinical diagnosis of CL have ranged from clinical picture and epidemiological data, isolating the amastigotes by microscopy of stained smears from skin touch specimens or biopsies to *invitro* culturing of the parasite (*Reed, 1996; Herwaldt, 1999*). These conventional methods are, however, limited in sensitivity, need an experienced hand and do not distinguish between *Leishmania* species which differ in virulence and, subsequently, may require different therapeutic regimes and control measures. For all this and over the last decade diagnostic tests based on molecular biology techniques i.e, PCR, were introduced and proved to be more sensitive and specific (Van Eys *et al.*, 1992; Wilson, 1995; Osman *et al.*, 1998).

L. major and L. tropica are restricted to the Old World (OW), mainly in the Mediterranean basin, East Africa, Indian subcontinent, and West and Central Asia . L. major CL is found in low lying arid and semiarid deserts (Klaus 1999). L. tropical CL, by contrast, is more common in urban areas and in villages in hilly rural areas (Klaus 1999). Examples for L. major foci are Jericho in Palestine (Al-Jawabreh et al., 2003 and 2004) and Sidi-Bozaid in Tunisia (Ben Ismail et al., 1997). As reviewed by Jacobson (Jacobson, 2003), examples for urban L. tropica foci are Baghdad in Iraq, Aleppo in Syria, Kabul in Afghanistan and Sanliurfa in South-east Turkey.

Within the past decade, the world's largest *L. tropica* focus was in Kabul (WHO, 2002). Other smaller foci for *L. tropica* can be found in Shiraz in Iran, Mosul in Iraq, Ashkhabad in Turkmenistan, and Taza in Morocco.

1.1.7. Treatment.

Simple CL due to *L.major* is mostly left to self-cure. In endemic areas, it is even preferable not to treat, so that long-term immunity can be acquired. Treatment is necessary when cosmetically or functionally important sites are involved. *L.tropica* infections generally require treatment. For local treatment, intralesional Pentostam (sodiumstibogluconate), ketoconazol, cryotherapy with liquid nitrogen or heat can be applied. For systemic treatment, pentavalent antimonal compounds (Sb) eg. Pentostam and Glucantime are used (Herwaldt, 1999; Norton *et. al.*, 1992; Hepburn, 2000). Resistance against pentavalent antimonals has become a serious problem, especially in India. As an alternative drug Amphotericin-B has proved to be effective too. The combinations of Paromomycin (Aminosidine) with Sb and interferon-γ with Sb arealso efficient and may help to reduce side effects of Sb compounds (less Sb is required) (reviewed by Berman, 1997).

1.2. Significance of the study.

Leishmainaisis disease is **on rise** in several countries in the World. Although, the disease is by law a reportable disease in Palestine, but nevertheless the disease seems to be greatly underreported. Therefore, it is

vital for understanding the epidemiological pattern of the disease distribution and for the prevention and control of the diseases to study distribution and factor affecting the diseases prevalence in Palestinian communities. Since Jenin district is known in literature to be the most affected area in the Palestinian territories, the study will focus on this district.

Chapter Two

Literature Review

2. Literature Review

2.1. Epidemiology and Environmental factors.

Cutaneous leishmaniasis is a vector borne disease caused by various members of the genus *Leishmania* parasite. Leishmaniasis is considered as a poverty-related disease. The endemic areas with leishmaniasis are usually identified by active or passive case reporting while the epidemic areas are usually identified by an early warning system. The distribution and epidemiology of both parasites is governed by several factors. The disease affects the poorest people and it is associated with conditions like malnutrition, displacement, poor housing, illiteracy, gender discrimination, weakness of the immune system and lack of resources. Environmental changes such as deforestation, building of dams, new irrigation schemes and urbanization, and the accompanying migration of non-immune people to endemic areas are linked to leishmaniasis (**Kroeger et al. 2002**).

2.2. Incidence of leishmaniasis in the World and in the Eastern Mediterranean region .

The clinical presentation ranges from simple cutaneous lesions to life threatening visceral forms. Currently, leishmaniasis occurs in four continents and is considered to be endemic in 88 countries, 72 of which are developing countries (WHOhttp://www.who.int/leishmaniasis/burden/en/.). Leishmaniasis is not only widely distributed in warm countries, but it is also prevalent in very different topographic areas. The disease is endemic

with about 1.5 million cases occurring each year (Centre for diseases control and prevention (CDC). Diseases & conditions. Leishmania infection (Leishmaniasis). Fact sheet. [Cited 2007 Sep 11]. Available from: http://www.cdc.gov/ncidod/parasites/leishmanai/factsht_leishmania.htm. In most of the endemic countries leishmaniasis is not a reportable disease (http://www.who.int/emc/diseases/ leish/leisdis1.html). New endemic foci have emerged over the past decades, epidemics are not controlled and endemic areas are spreading due to development and population shifts (Desjeux, 1999). In western countries the incidence is increasing due to HIV-Leishmania coinfection and tourism. In recent years coinfection with HIV became a serious threat in south-western Europe with 1.5-9.5% of AIDS patients being affected.

In the Eastern Mediterranean region (EMR), cutaneous and visceral Leishmaniasis are reported from 14 of the 22 countries of the region, namely Afghanistan, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Libyan Arab Jamahiriya, Morocco, Pakistan, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia and Yemen (Postigo, 2010). In these countries, outbreaks of leishmaniasis are tend to occur every 10 years (Postigo, 2010). In 2008, about 100,000 new cases of CL were reported from some of the EMR countries including Palestine. (Postigo, 2010). The estimated number of cases of CL caused by *L. tropica* in Middle East and North Africa countries is reported to be 40,000 (Hotez et al., 2012).

2.3. Leishmaniasis in Palestine

CL has been first reported in Jericho since the area was used to be free of leishmaniasis as reported by residents until the 1967 War. This was due to be a result of spraying against malaria by DDT. However, reports from Israeli soldiers post 1967 War revealed that the area is hyperendemic. *Leishmania major* accounts for the

majority of infections with *Leishmania* in the country. It is endemic in the Jordan Valley, the Jericho area, along the Dead Sea, in the Arava and the Negev. CL caused by *L.major* has been thoroughly studied over many years, and the reservoir animal species (*P.obesus*, *M.crassus*) as well as the vector species (*Ph.papatasi*) have been identified (**Schlein** *et al.*, **1982**; **1984**).

Leishmania tropica is endemic in a number of semiarid hilly areas in central and northern Israel as well as in the northern West Bank (Samaria), the Jenin district being a major endemic area (**Abdeen** *et al.*, 2002). The species has never been finally confirmed, but the hillyenvironment was highly suggestive of a focus of *L.tropica*.

The epidemiology of leishmaniasis has been also studied in Palestine and two forms of leishmaniasis have been reported. One is the CL caused by *L. major* or *L. tropica* and the other is VL caused by *L. infantum*. Leishmaniasis in general is reported in all Palestinian districts except Gaza strip with an official incidence rate in the West Bank of more than 10 per

100,000 in 2003 (Klaus et al., 1994; Baneth et al., 1998; Abdeen et al., 2002; Anders et al., 2002; Al-Jawabreh et al., 2004, Jaffe et al., 2004, Schoenian 2003; Ministry of Health, 2004). The annual incidence of CL was studied in Jerusalem and its neighboring areas and it has been reported that the annual incidence of CL increased from 0.13 in 1999-2003 to 9.7 per 100,000 in 2004-2005 (Singer et al. 2008). The highest incidence was reported from district of Tiberias and found to be 62.5 per 100,000 (Vinitsky et al. 2010).

The epidemiology of CL in the Jericho district has been profoundly studied by Al-Jawabreh (2000). In this context, Al-Jawabreh et al. (2004) reported the emergence of L. tropica in Jericho (A'riha) in the period between 1997-2002. Of the 107 dermal samples tested, around 50% were infected with *L. tropica* and the rest by *L. major* as revealed PCR technique. *L. tropica* is endemic in a number of areas in the northern West Bank, the Jenin district being a major endemic area (Abdeen et al., 2002). According to Sawalha (2001) more than 700 cases of CL have been reported from many single foci in the northern West Bank over the last decade. The causative species has not been identified, but the geographical area suggests *L. tropica*. CL caused by *L. tropical* is less prevalent than *L. major* (see Schnur et al., 2004).

L.d.infantum is an emerging disease in the northern West Bank. Several cases of VL has been reported from the area of northern West Bank (Badr et al., 2005; Abdeen et al., 2002). Most cases were reported in the Jenin

district, followed by Hebron, Tulkarem and Ramallah. Predominantly children between 1 and 6 years of age were affected (**Abdeen** *et al.*, **2002**, **Giladi** *et al.*, **1985**, **Qubain** *et al.*, **1997**). Other two reports of VL has been published from Bal'a village, 5 KM East of Tulkarm city (Qubain et al., 2009) and from Hebron district (**Amro et al., 2009**).

The epidemiology of leishmaniasis in [Israel] has been reviewed by Giladi et al., 1985). CL and VL forms are reported long time ago in [Israel], however, epidemiological studies showed that they are re-emerging as important public health problems in areas long believed to be disease free (Jaffe et al., 2004). For example several reports have indicated CL, caused by L. tropica, has become a significant problem in northern [Israel] and West Bank of Palestine (Jaffe et al., 2004; Amro et al., 2009; Al-Jawabreh et al., 2003; Schnur et al., 2004). VL has been also reported from different parts of Palestine including Hebron (Amro et al., 2009) and Jenin districts (Abdeen et al., 2002).

Chapter Three Material and Methods

3.1. Patients and study area.

All of north Palestinian districts (Jenin, Nablus, Tubas, Tulkarm, Salfeet and Nablus, extend over an area of more than 593 km², with a population density of 73 person per km² and a total population of more than 40,909 (Palestinian Central Bureau of Statistics, 2005). Jenin and Tubas districts are located in the northren part of the West Bank. There have 96 localities and covers an area of 592 km² with altitudes ranging between 90 and 750 meters above sea level (palestinain central bureau of statistics, 2007). Jericho, a strip of land extends from the Dead Sea and Jerusalem in the south to Nablus. Tubas and Jenin in the north and from the River Jordan in the east to the hills of Ramallah and Nablus in the west, is a low-lying (244-398 m below sea level) arid to semi-arid area located between 29°-33° north of the equator. The Palestinian population living in northern part of West Bank work as farmers, government employees and nomadic Bedouin shepherds who roam the area all the year round.



Figure 9. Map of the Palestinian governorates according to Palestinian classification.

3.2. Design of the study:

The research design of this study is cross-sectional descriptive retrospective design. This design was chosen to investigate the factors that lead to the increase of CL cases in the northern West Bank. Although the study is descriptive, it attempt to put the problem in prospective by showing the relative degree to which different districts are affected, how the patterns of the disease occurrence vary between different areas .

3.3. Sample collection:

Patient data sheets. Data of each referred patient has been collected from the dermatological private clinics and files from August 2000 to August 2010 in the preventive medicine departments in all of the districts. The tool used in this study is a questionnaire filled in by the author directly or by telephone interviewing the patients. Data are filled from the file. However, if there are certain information missing, then author has called the patient and filled missed information. In case some patients can not be contacted, then the file has been excluded. The questionnaire includes demographic, clinical, diagnostic, and epidemiological questions. The questionnaire has been designed by the author and thus it has been validated by a pilot study on 30 files. After analysis of data, the questionnaire was used to collected relevant data. It is worth mentioning that the files used in the pilot study have not been included in this study. It has been also designed to be used friendly with a computerized input interface and analysis by SPSS.

Inclusion criteria:

All files for patients who have a file in the preventive medicine departments within 10 years (2000-2010)

The exclusion criteria:

Files for patients in the period before 2000 and after 2010.

Ethical consideration:

Permission has been sought from the Internal Review Board (IRB) at An-Najah National University and from the Ministry of Health.

Statistical analysis

Collected data was analyzed using the statistical package for social sciences program (SPSS) version 16. Descriptive results were expressed as frequencies and percentages.

Chapter Four

Results

4.1. Distribution of study participants.

The total number of study sample was 1150 with mean age of 23.9 ± 19.1 yrs (min 1yr and max 90 yrs). Table 1 summarizes age distribution of the study participants. Of those 54.3% (624/1150) were males.

Table 1. Age categories of study participants.

Age (yrs)	Frequency	
	Number	%
<18	629	54.7
18-49	374	32.5
>49	147	12.8
Total	1150	100

They were distributed into 5 distinct districts as demonstrated by figure 10. More than 50% of samples were from Jenin district. The district incidence rate in Nablus was 532 per 100,000. Qaliqilia had the least rate

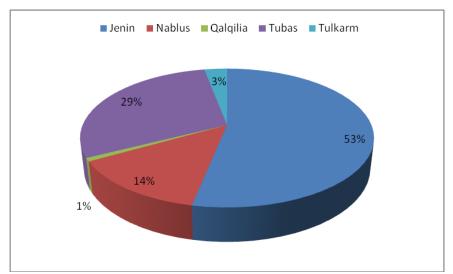


Figure 10. Distribution of study samples by residence (Total number of study samples is 1150).

4.2. Year of infection and districts.

Table 2. Number of patients with cutaneous leishmanisis distributed into districs of North west Bank.

	2. Number of patients with entancous reishmanishs distributed into district of North west Dank.											
District	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	Total
Jenin	55	116	85	69	18	34	35	52	80	26	41	611(53%)
Nablus	14	12	10	11	4	9	8	20	37	14	17	156 (13.6)
Qaliq	0	0	1	0	0	1	0	5	2	0	0	9 (0.8%)
Tubas	13	22	26	32	4	14	16	19	65	66	61	339 (29.5%)
Tulkar	2	3	4	6	1	4	2	5	4	3	0	34 (3%)
Total												1150

4.3. Demographic and epidemiologic characteristics of CL patients in Northern West Bank, Palestine (2000-2010)

Figure 11 demonstrates the distribution of sex of patients enrolled in the study. About 54% of them were males.

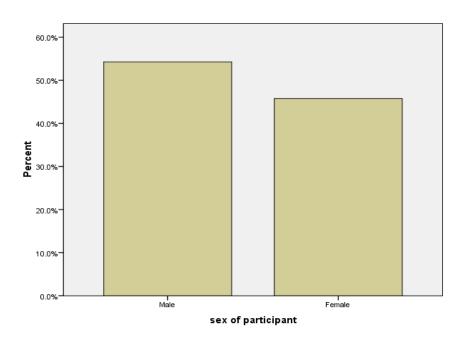


Figure 11. Distribution of sex of patients with cutaneous leishmaniasis.

4.4. Place of residence

Figure 12 demonstrates the distribution of patients with respect to area of residence. About 78.7% (902/1150) respondents are living in the village. Of those 73.3% (847/1150) are living in the peripheral of the village. In comparison, 16.7 (192/1150), about 2% (25/1150) and 2% (26/1145) were living in city, refugee camps and Badya, respectively (figure 12).

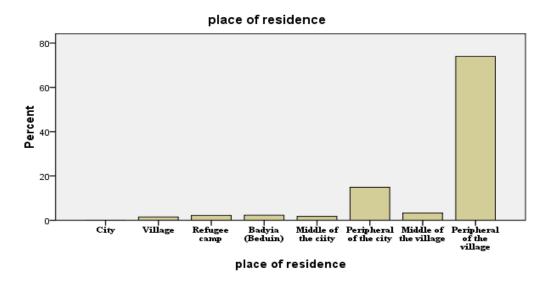


Figure 12. Place of living of patients with CL.

4.5. profession

The majority of patients were found to be students (39.5% (454/1150) (figure 13). Patients who are farmers constituted about 12% (144/1150) of the study samples. Housewives were 19.2% (221/1150) of study samples who contracted CL.

Profession in categories

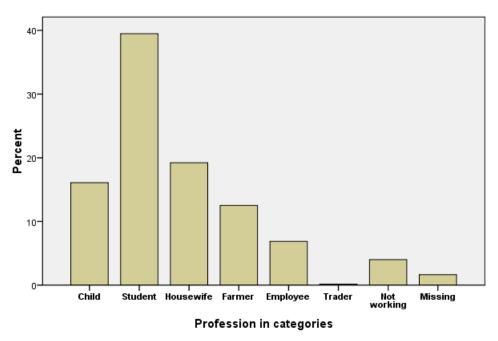


Figure 13. The profession of patients with CL in North West Bank.

4.6.Site of infection

Figure 14 demonstrates site of infection. About 74% (854/1150) of our participants have infections on the peripherals (exposed areas on hands, legs). The second site was found to be the face (24%).

site of infection

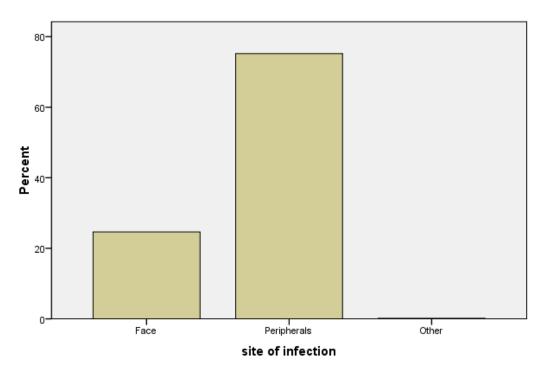


Figure 14. Site of infections of CL as found on study participants.

4.7. Number of nodules

Exploring number of nodules per patient was performed. Results as demonstrated by figure 15 showed that majority of patients have just one nodule (68.4% (787/1150). Only 3% (34/1150) had more than two nodules. The rest of patients (26.2%, 305/1150) had two nodules. There were missing data for 24 patients.

number of infection nodules

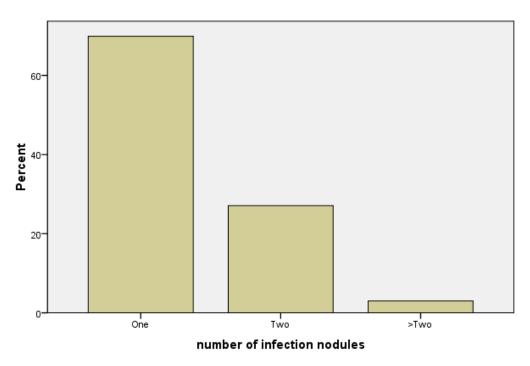


Figure 15. Distribution of nodules among patients with CL in North of west Bank

4.8. Type of animals living in contact with patients with CL

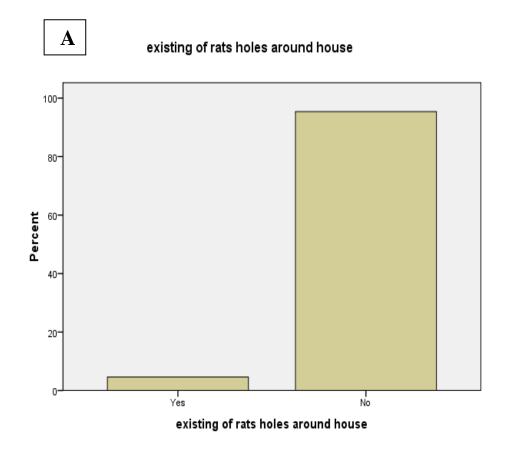
Table 3 summarizes the distribution of domestic animals which are in contact with CL patients.

Table 3. Distribution of domestic animals near patients with CL.

Animal	Frequency [No (%)]
Cows	29 (2.5)
Goats	101 (8.8)
Sheeps	249 (21.7)
Chickens	38 (3.3)
ND	733 (63.7)
Total	1150 (100)

4.9. Existing of dogs and rats around the area of patients with CL

Our data showed that 95% (1093/1150) of patients with CL reported no holes of rats in the area where they live (Fig. 16A). When respondents were asked whether they have seen rats around their houses, 6.6% (75/1150) have confirmed the presence of those non-domestic animals while the majority (76.4%;879/1150) reported no rats near their residence (fig. 16B)



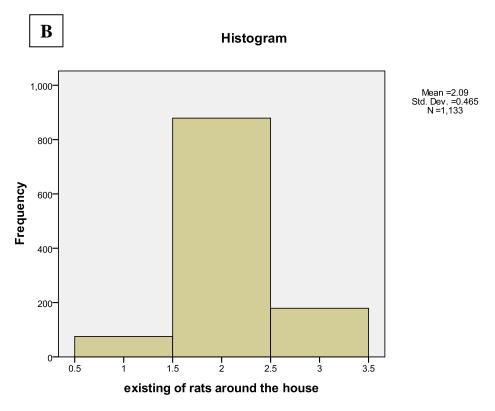


Figure 16. Existing of rats (A) or holes for rats (B) where patients with CL live.

There were 43.2% (497/1150) of respondents who saw dogs around their homes (Fig 7). However, 48% (553/1150) of respondents were not sure if they have seen dogs around.

number of dogs around the house

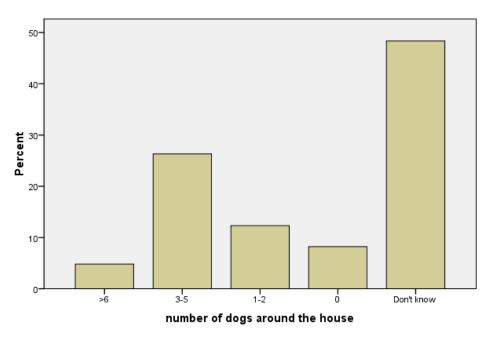


Figure 17. Existence of dogs around the patients with CL houses (numbers in the X-axis represents number of dogs).

4.10. Environmental hazards around where people live

In order to relate the presence of the leishmania vector in the area where patients with CL live, the study has been concerned with accumulation of waste in the area. Figure 18 shows clearly that around 85% of patients suffered from accumulation of waste near where they live.

does the solid waste accumulate around the house

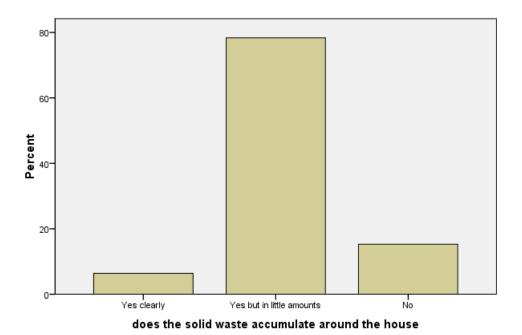


Figure 18. Accumulation of waste around the area where patients with CL are living.

4.11. Presence of screens on windows

The data in this study showed that around 87% of participants (1007/1150) had window screens (nets) in their houses (fig.19).

existing of window's cover in the house

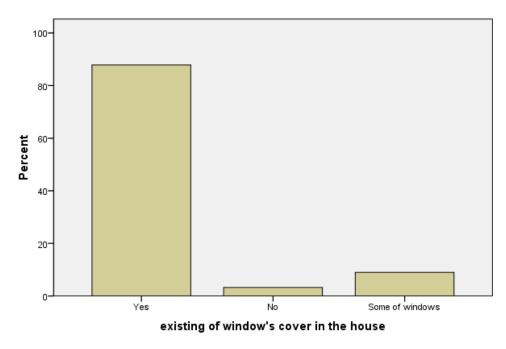


Figure 19. Presence of window screens (nets) in the houses of patients with CL

4.12. Use of insecticides inside homes of study participants

Participants have been asked about use of insecticides in their homes. Although 92 of participants were occasionally using insecticides, only 4% (55/1150) of those participants reported using insecticides all the time (fig20).

do you use the pesticides at home

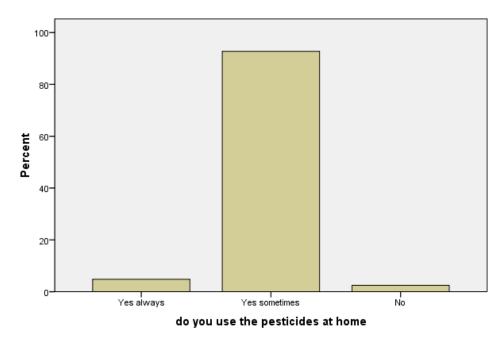


Figure 20. Use of insecticides insides houses of patients with CL.

4.13. Use of Namosiya by participants

Participants have been asked about using namosiya in their sleep. Almost none of respondents (0.2%) were using cover (namosiya) in their beds (fig21)

namosyia use during sleeping

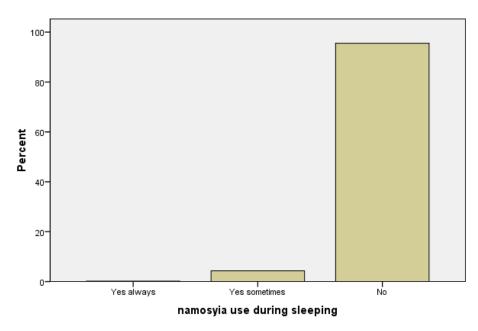


Figure 21. Use of net covers (namosiya) by patients of CL in their beds.

4.14. Geography of houses and presences of caves around patients residences

The geography of houses of study participants were of focus of this study. It has been found that around 83% (964/1150) of study samples live on mountain valleys while only 4.5% (52/1150) were living on sahel (fig. 23).

The presence of cracks and caves around the residence of patients with CL was investigated. Clearly more than 50% of patients have caves or cracks near where they live. 41% of them have those caves or cracks but at longer distances of their homes (fig. 24).

geography of house

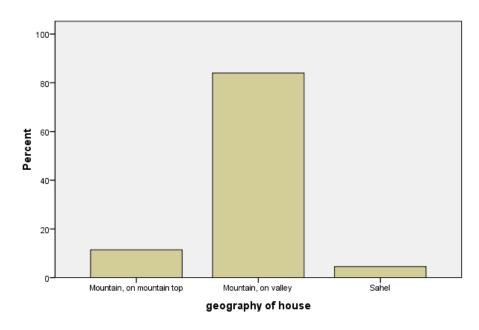


Figure 22. Distribution of patient's houses.

pres of kohoof and tassadoaad sagryia around the house

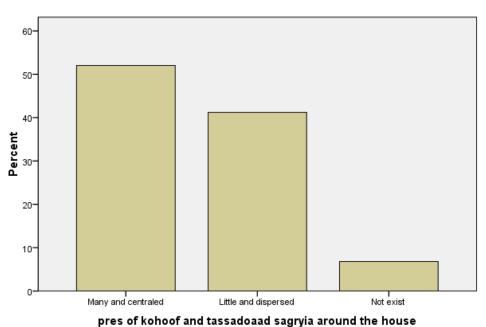


Figure 23. Presence of caves and cracks near the residence of patients with CL.

Chapter 5

Discussion

5.1.Discussion

Leishmania spp are the causative agents of leishmaniasis, a parasitic disease with wide range of symptoms including cutaneous (CL), mucocutaneous and visceral (VL) leishmaniasis. The disease currently affects around 350 million people in more than 88 countries worldwide (Desjeux, 2001). CL in Palestine, similar to other parts of the eastern Mediterranean basin is known to be caused by both L. major and L. tropica. Public health control measures in any country are strongly dependent on the information coming from the surveillance systems. On CL, for example, the WHO Expert Committee report (1990) stated that passive case detection, treatment and reporting should be the basis for a control program. Notification of the ministry of Health (MOH) of leishmaniasis in Palestine is required by law. Therefore, this study uses reported cases of CL in northern parts of West Bank of Palestine to MOH in order to get insights about possible causes of infection by this disease.

Leishmaniasis is endemic in areas of tropics, subtropics, in southern Europe, in settings ranging from rain forests in the Americans to deserts in western Asia, and from rural to periurban areas. CL is considered as an emerging disease to the area since it has been thought for long time that the disease was eradicated.

There are a number of ecological, clinical, epidemiological and entomological studies concerning the leishmaniasis that have been conducted in the area (Jaffe et al. 2004; Al-Jawabreh et al 2004). However,

from our observation the number of cases of CL has increased in the area of north West Bank. Thus, it was of great importance to analyse the causes of this increase in the area.

There were 1150 patients with CL included in this study in the period between 2000 and 2010. Thus, this study confirms that an important and active focus of leishmaniasis has been in existence in northern of West Banks, particularly in Jenin district. Other studies have previously reported the endemicity of both VL and CL in Palestine including Jericho, Jerusalem, Hebron, Safed, Negev (Abdeen eta., 2000; Vinititsky et al., 2010; Singer et al., 2008; Jaffe et al., 2004; Al-Jawabreh et al., 2003; Amro et al., 2009). The mean age of our study participants is about 24 years. About 50% of patients were below 18 years old. It seems that children are the most affected age group. Similar finding was reported also by a study on VL in Jenin district (Abdeen et al (2002). Al-Jawabreh et al (2003) has reported similar findings where high rate of infection in children. It is expected that children will be easily infected in hyperendemic situation and we would expect that this gives children a protective immunity as adults.

The incidence of CL was found to be the highest in Tubas district followed by Jenin. In Tubas district, incidence of CL showed dramatic increase by5-fold between 2000 and 2010. Incidence in other parts of West Banks as indicated by this study is low. Reported incidence in West Bank for 2003 is 10 per 100,000 (Klaus *et al.*, 1994; Baneth et al., 1998; Abdeen *et al.*,

2002; Anders et al., 2002; Al-Jawabreh et al., 2004, Jaffe et al., 2004, Schoenian 2003; Ministry of Health, 2004). This finding is in agreement with epidemiological reports of the area. For example, incidence in [Israel] was reported to be stable throughout the 1990 0.5-2.5/100,000 (Leventhal et al. 2001). However, other reports found high incidence of CL214/100,000 in 2004-2005) in other parts of [Israel] (Singer et al. (2008). Several studies have reported the endemicity of leishmanisis and sand fly vector in Jordan valley and Jericho (Al-Jawabreh et al., 2003; Jaffe et al., 2004; Janini et al., 1995). Incrimination of Phlebotomus papatasi as vector of Leishmania major in the southern Jordan Valley. Janini et al., 1995).

Tubas and part of Jenin district is very close to Jordan valley. Therefore, it is expected to find high incidence in these areas. The increase of incidence in recent years may be explained by advance in development and animal production activities as well as for better diagnosis. Additionally, reports has indicated the presence of animal reservoirs and the presence of sand fly vector proven or suspected to be vectors of CL in other parts of Middle East and Mediterranean are also present in Jenin and Tubas areas (Abdeen et al. 2002).

More than 70% of the study participants were living in villages and peripheral of villages. Similar finding with regard with eco-distribution of leishmaniasis was published where L. tropica is more common in suburbs and villages (Jacobson et al., 2003). Vinitsky et al (2010) concluded also

that most of patients with CL were living in the city outskirts. Others have reported that the infection occurs both in old housing and new suburban settlements and also in peripheral villages (**Postigo**, **2010**).

With regard of site of infection, the results showed that more than two third of our patients have their infection on their peripheral areas (hands and legs). About 25% of patients have their infection is on face. In other studies, it has been found that face and head are more affected in children and limbs were more affected in adults (Al-Jawabreh et al., 2003). The disagreement in results may be explained that children stay homes at night. It is well known that the activity of sand flies vectors is at night. Most of our patients use nets at their windows. This should protect them from infection by sand fly vector. This result may indicate that infection of patients (mostly) children are infected outside their houses. we should also not conclude that all nets are closed at night.

The current study showed that about 40% of participants reported dogs around their homes. Many patients have seen rat holes near where they live. Both dogs and rats are known as reservoir to CL taking into consideration that our dogs are mostly stray dogs. Sandfly vector feeds on a wide variety of hosts, including both mammals and birds. It is well known that fat sand rat *Psammomys obesus* maintains *L. major* in most foci in different countries from morocco in West to Syria and Saudi Arabia in the east. We do not know about the size of distribution of this gerbil in the area of the study. Therefore, we would recommend further studies on this aspect.

Dogs have reported as reservoir to the anthroponotic CL, although, it is thought that this is an incidental host and that the only host is human (Postigo, 2010). We would also recommend to analyze the role of dogs in transmission of CL in the study areas.

The epidemiology of CL in the Palestine and neighbouring countries appears to be undergoing a transition. Several factors, both environmental and ecological, may have contributed to the increase in CL incidence in the area particularly in Jenin districts during the period of 2000-2010. These include the expansion of towns and villages, the establishment of new settlements, and increase agricultural and poultry production. These conditions have led to an increase in refuse and solid waste providing good habitat to the vector sand fly and also attracting stray dogs and wild caned reservoir hosts.

5.2. Conclusion

The current study confirms the area of north West Bank is endemic with CL. Tubas and Jenin were found to be hyperendemic with CL since they showed high level of infection as depicted by the incidence rate of infection. Most of our patients were children of less than 18 years of old. Most of our participants are living in suburban areas. Dogs and rats are seen near residence of CL patients.

The high incidence of CL in north of West Bank and stabilization of this incidence necessitate the adoption of control measures by Palestinian authorities to tackle this problem.

5.3. Recommendations

Based on the results of this study we recommend the following

- 1. Expand this survey to include other parts of West Bank
- 2. To study the vector reservoir in the area in order to have clear insight on transmission of CL
- 3. The high incidence of CL in the area of study, particularly Jenin and Tubas areas make it urgent for health authorities to put measures and control program to eradicate *Leishmania* vector and reservoirs.
- 4. We strongly recommend ministry of health to establish surveillance system to ensure monitoring of leishmaniasis trends in the districts to permit the detection of new emerging foci and allow the monitoring of spatial dynamics of different forms of leishmaniasis, including VL, in order to better conduct preventive measures.

References

- Abdeen, Z. A., Sawalha, S. S., Khanfar, H. M., Shtayeh, M. S., Warburg, A., Greenblatt, C. L., Jaffe, C. L, Baneth, G. (2002). Epidemiology of human and canine visceral leishmaniasis in the Jenin district, West Bank, 1989-1998. Am. J. Trop. Med. Hyg.; 66(4):329-33.
- Alexander J, Satoskar AR, Russell DG. (1999). Leishmania species: models of intracellular parasitism. J Cell Sci. Sep;112 Pt 18:2993-3002
- Al-Gindan Y, Kubba R, El-Hassan A, Omar, A. H., Kutty, M. K., and Saeed, M. B. (1989). Dissemination in cutaneous leishmaniasis. 3.
 Lymph node involvement. Int. J. Dermatol.; 28: 248 –54.
- Al-Jawabreh, A., Barghuthy, F., Schnur, L. F., Jacobson, R. L., Schoenian, G. & Abdeen, Z. (2003). Risk assessment of cutaneous leishmaniasis in the endemic area of Jericho in Palestine. East. Med. Hlth. J.; 9 (4): 805-15.
- Al-Jawabreh, A., Schnur, L. F., Nasereddin, A., Schwenkenbecher, J. M, Abdeen, Z., Barghuthy, F., Khanfar, H. Presber, W and Schoenian, G. (2004). The recent emergence of Leishmania tropica in Jericho (A'riha) and its environs, a classical focus of Leishmania major. Trop. Med. Int. Hlth. 9 (7): 812–816.

- Amro A, Azmi K, Schönian G, Nasereddin A, Alsharabati MB, Sawalha S, Hamarsheh O, Ereqat S, Abdeen Z. (2009). Epidemiology of paediatric visceral leishmaniasis in Hebron district, Palestine. Trans R Soc Trop Med Hyg. Jul;103(7):731-6.
- Anders, G., Eisenberger, C. L., Jonas, F., and Greenblatt, C. L. (2002).
 Distinguishing Leishmania tropica and Leishmania major in the
 Middle East using the polymerase chain reaction with kinetoplast
 DNA-specific primers. Transactions of the Royal Society of Tropical
 Medicine and Hygiene, 96: 87-S92
- Arda, H. M. and Kamal, A. (1983). A report on cutaneous
 Leishmaniasis in the West Bank of Jordan. Jordan Med. J.; 17 (1): 57-63.
- Ashford, R. W. (2000). The leishmaniasis as emerging and remerging zonooses. Int. J. Parasitol.; 30: 1269-1281
- Bader KA, Schnur LF, Nasereddin A, Pratlong F, Dedet JP, Shaheen L, Yousef O, Greenblatt CL. (2005). Palestinian infantile visceral leishmaniasis caused by a genetic variant of Leishmania infantum belonging to a new zymodeme. Trop Med Int Health. 2005 Jun;10(6):618-20.
- Belli A, García D, Palacios X, Rodriguez B, Valle S, Videa E, Tinoco E,
 Marin F, Harris E. (1999). Widespread atypical cutaneous

- leishmaniasis caused by Leishmania (L) chagasi in Nicaragua. Am. J. Trop. Med. Hyg. 61(3), 380-385
- Ben-Ismail, R., Garraoui, A., Chaded, M.K., Ben Salah, A., Abdouli, M., Zaafouri, B., Khadhraoui, B., Ftaiti, A., Sidhom, M. & Dellagi, K. (1997). Environmental changes to control Leishmania major cutaneous leishmaniasis in the epidemic focus of Sidi Bouzid (Tunisia)First World Congress on Leishmaniosis. Istanbul, May 5ß9, 1997. Acta Parasitologica Turcica, 21, 138.
- Bray, R. S. (1987). Note on the history of cutaneous leishmaniasis in the Mediterranean and Middle East area. Parassitologia; 29 (2-3):175-xxx.
- El Tai, N. O., Osman, O. F., El Fari, M., Presber, W. and Schonian, G. (2000). Genetic heterogeneity of ribosomal internal transcribed spacer in clinical samples of Leishmania donovani spotted on filter paper as revealed by single-strand conformation polymorphisms and sequencing. Trans. R. Soc. Trop. Med. Hyg.; 94, 1-5.
- Giladi M, Danon YL, Greenblatt C, Schinder E, Nili E. (1985). Keziot-a new endemic site of cutaneous leishmaniasis in Israel. An
 epidemiological and clinical study of a non-immune population
 entering an endemic area. Trop Geogr Med. Dec;37(4):298-303.
- Gillis D, Klaus S, Schnur L, Piscopos, P., Maayan, S., Okon, E. and Engelhard, D. (1995). **Diffusely disseminated cutaneous Leishmania**

- major infection in a child with acquired immunodeficiency syndrome. Ped. Infect. Dis. J.; 14:247–9.
- Hatam G.R., Hosseini S.M.H., Ardehali S. (1997). Dermotropic isolates
 of Leishmania infantum in Iran. Trans. R. Soc. Trop. Med. Hyg. 91,
 440
- Herwaldt, B. L. (1999 a). Leishmaniasis. Lancet; 354: 1191-1199
 Jacobson, R. L. (2003). Leishmania tropica (Kinetoplastida: Trypanosomatidae) a perplexing parasite. Folia Parasitol.; 50: 241–250.
- Jaffe, C. L, Baneth, G. (2002). Epidemiology of human and canine visceral leishmaniasis in the Jenin district, West Bank, 1989-1998.
 Am. J. Trop. Med. Hyg.; 66(4):329-33.
- Jaffe, C. L., Baneth, G., Abdeen, Z., Schlein, Y. and Warburg, A. (2004).
 Leishmaniasis in Israel and the Palestinian Authority. Trends
 Parasitol.; 20:328-332.
- Klaus S, and Frankenburg S. (1999). Cutaneous Leishmaniasis in the Middle East, Clin. Dermatol.; 17:137–141
- Klaus S, Axelrod O, Jonas F, Frankenburg S, (1994). Changing patterns of cutaneous leishmaniasis in Israel and neighbouring territories. Trans. R. Soc. Tro.p Med. Hyg.; 88: 649–650

- Klaus S, Frankenburg S. (1999). Cutaneous leishmaniasis in the Middle East. Clin Dermatol. 1999 Mar-Apr;17(2):137-41
- Meredith, S. E., Zijlstra, E. E., Schoone, G. J., Kroon, C. C., Van Eys, G. J. Schaeffer, K. U., el- Hassan, A. M. and Lawyer, P. G., L. (1993).
 Development and application of the128 polymerase chain reaction for the detection and identification of leishmania parasites in clinical material. Arch. Inst. Pasteur Tunis. 70: 419-431.
- Ministry of Health-PHIC. (2004). Health indicators in Palestine 2003, http://www.moh.gov.
- Morsy, A. T. (1996). Cutaneous leishmaniasisin Egypt (Review and comment). J. Egypt Soc parasitol.; 26 (1)
- Naggan, L., Gunders, A. E., Dizian, R., Dannon, Y., Shibolet, S., Ronen,
 A., Schneeweiss, R. & Michaeli, D. (1970). Ecology and attempted
 control of cutaneous Leishmaniasis arround Jericho in the Jordan
 Valley. J. Infec. Dis.; 427-431.
- Nuwayri-Salti N, Baydoun E, Alema- Munoz MM, Kreutzer RD. (1994)
 Identification of Leishmania isolates from a Lebanese population.
 Am. J. Trop. Med. Hyg. 51(1), 98-101
- Osman, O. F, Oskam, L., Kroon, N. C., Schoone, G. J., Khalil, E. T., El
 Hassan, A. M., Zijlstra, E. and Kager, P. A. (1998). Use of PCR for

- diagnosis of post kala-azar dermal leishmaniasis (PKDL). J. Clin. Microbiol.; **36 (6)**: 1621-1624.
- Oumeish, O. Y. (1999). Cutaneous Leishmaniasis: A Historical Perspective. Clin Dermatol. 17:249–254.
- Palestinian Central Bureau of Statistics (PCBS), (2005). Population
 Projections in the Palestinian Territory, Revised Series. Ramallah-Palestine.
- Peters W, Bryceson A, Evans DA, Neal RA, Kaye P, Blackwell J, Killick-KendrickR, Liew FY. (1990). Leishmania infecting man and wild animals in Saudi Arabia. 8. The influence of prior infection with Leishmania arabica on challenge with L. major in man. Trans R Soc Trop Med Hyg. 1990 Sep-Oct;84(5):681-9.
- Qubain HI, Saliba EK, Oskam L. (1997). Visceral leishmaniasis from Bal'a, Palestine, caused by Leishmania donovani s.1. identified through polymerase chain reaction and restriction fragment length polymorphism analysis. Acta Trop. Oct 14;68(1):121-8.
- Ramirez, J. R., Agudelo, S., Muskus, C., Alzate, J. F., Berbrich, C., Barker, D., and Velez, I. D. (2000). Diagnosis of Cutaneous Leishmaniasis in Colombia: the Sampling Site within Lesions Influences the Sensitivity of Parasitologic Diagnosis. J. Clin. Microbiol.; 38 (10):

- Ramos-Santos C, Hernandez-Montez O, Sanchez-Tejeda G, Monroy-Ostria A. (2000). Visceral leishmaniasis caused by Leishmania (L.) mexicana in a mexican patient with human immunodeficiency virus infection. Mem. Inst Oswaldo Cruz 95(5), 733-737
- Reale A, Maxia L, Vitale F, Glorioso NS, Caracappa S, Vesco G.
 Detection of Leishmania infantum in dogs by PCR with lymph node aspirates and blood. J. Clin. Microbiol. 37(9) (1999), 2931-2935
- Reed, S. G. (1996). Diagnosis of Leishmaniasis. Clinics in Dermatology, 24:471-47.
- Rioux, J. A., Lanotte, G., Serres, E., Pratlong, F., Bastien, P. and Perieres, J. (1990). Taxonomy of Leishmania. Use of enzymes.
 Suggestions for a new classification. Ann. Parasitol. Hum. Comp.; 65: 111–125.
- Rittig MG, Bogdan C. (2000). **Leishmania-host-cell interaction: complexities and alternative views**. Parasitol Today. Jul;16(7):292-7.
- Rodgers, M. R., J. Stephen, and D. F. Wirth. 1990. Amplification and diagnosis of leishmania. Exp. Parasitol. 71:267–275.
- Sacks, D. L., Kenny, R. T., Kreutzer, R. D., Jaffe, C. L., Gupta, A. K., Sharma, M. C.,
- Saliba EK, Saleh N, Oumeish OY, Khoury S, Bisharat Z, al-Ouran R.
 (1997). The endemicity of Leishmania tropica (zymodeme MON-

- **137**) in the Eira-Yarqa area of Salt District, Jordan. Ann Trop Med Parasitol. 1997 Jul;91(5):453-9.
- Salman S.M., Rubeiz N.G., Kibbi A.-G. (1999). Cutaneous
 Leishamaniasis: Clinical features and diagnosis. Clin. Dermatol.
 17(3), 291-296solates from a Lebanese population. Am. J. Trop. Med.
 Hyg. 51(1) (1994), 98-101
- Satti, M. B., El-Hassan, A. M., Al-Gindan, Y., Osman, M. A., Al-Sohaibani, M. O. (1989). Peripheral neural involvement in cutaneous leishmaniasis. A pathologic study of human and experimental animal lesions. Int J Dermatol. 28(4):243-7.
- Schlein, Y., Warburg, A., Schnur, L. F., Gunders, A.E., Leishmaniasis in the Jordan
- Valley II. (1982). Sandflies and transmission in the central endemic area. Trans. R. Soc. Trop. Med. Hyg; **76**(5), 582-586
- Schlein Y, Warburg A, Schnur LF, Le Blancq SM, Gunders AE. (1984).
 Leishmaniasis in Israel: reservoir hosts, sandfly vectors and leishmanial strains in the Negev, Central Arava and along the Dead Sea. Trans R Soc Trop Med Hyg.;78(4):480-4
- Schnur, L. F., Zuckerman, A., Greenblatt, C. L.(1972). Leishmanial serotypes as distinguished by the gel diffusion of factors excreted in vitro and in vivo. Israel. J. Med. Sci.; 8: 932-942.

- Schonian, G., Nasereddin, A., Dinse, N., Schweynoch, C., Schallig, H.
 D., Presber, W. and Jaffe, C. L. (2003). diagnosis and characterization
 of Leishmania in local and imported clinical samples. Diagn
 Microbiol Infect Dis.; 47(1):349-58.
- Schonian, G.; Schweynoch, C.; Zlateva, K.; Oskam, L.; Kroon, N.;
 Gräser, Y. & Presber, W. (1996). Identification and determination of
 the relationship of species and strains within the genus Leishmania
 using single primers in the polymerase chain reaction. Mol. Biochem.
 Parasitol.; 77, 19-29.
- Schnur LF, Nasereddin A, Eisenberger CL, Jaffe CL, El Fari M, Azmi K, Anders G, Killick-Kendrick M, Killick-Kendrick R, Dedet JP, Pratlong F, Kanaan M, Grossman T, Jacobson RL, Schonian G, Warburg A. (2004). Multifarious characterization of leishmania tropica from a Judean desert focus, exposing intraspecific diversity and incriminating phlebotomus sergenti as its vector. Am J Trop Med Hyg. Apr;70(4):364-72.
- Sinha, S. P., Neva, F. A. and Saran, R. (1995). Indian kala-azar caused
 by Leishmania tropica. The Lancet, 345.
- Van Eys, G. J. J. M., G. J. Schoone, N. C. M. Kroon, and S. B. Ebeling. (1992). Sequence analysis of small subunit ribosomal RNA genes and its use for detection and identification of Leishmania parasites. Mol. Biochem. Parasitol.; 51:133–142.

- Vardy, D., Frankenburg, S., Goldenhersh M, Leibovici, V. & Klaus, S. N. (1993). Unusually extensive disease caused by Leishmania major parasites. Clin Exp. Dermatol.; 18:36–40.
- WHO. 1991. "Information on the Epidemiology and Control of the Leishmaniasis by Country or Territory." WHO/Leish/91, Geneva.
- WHO. 1996. "Manual on Visceral Leishmaniasis Control." WHO/6531–6535. Leish/96–40, Geneva.
- WHO. 1998. "Leishmania and HIV in gridlock." WHO/UNAIDS report, 12–25, Genev.
- Strelkova MV. (1996). Progress in studies on Central Asian foci of zoonotic cutaneous leishmaniasis: a review. Folia Parasitol (Praha). 1996;43(1):1-6.
- Yaghoobi-Ershadi MR, Javadian E. (1996). Seasonal variation of Leishmania major infection rates in sandflies from rodent burrows in Isfahan province, Iran. Med Vet Entomol. 1996 Apr;10(2):181-4.
- Marlet MV, Sang DK, Ritmeijer K, Muga RO, Onsongo J, Davidson RN.
 (2003). Emergence or re-emergence of visceral leishmaniasis in areas
 of Somalia, north-eastern Kenya, and south-eastern Ethiopia
 in 2000-01. Trans R Soc Trop Med Hyg. Sep-Oct;97(5):515-8.

- Dereure J, Rioux JA, Gallego M, Perières J, Pratlong F, Mahjour J,
 Saddiki H. (1991). Leishmania tropica in Morocco: infection in dogs. Trans R Soc Trop Med Hyg. Sep-Oct;85(5):595.
- Aljeboori TI, Evans DA. (1980). Leishmania spp. in Iraq.
 Electrophoretic isoenzyme patterns. II. Cutaneous
 leishmaniasis. Trans R Soc Trop Med Hyg. 1980;74(2):178-84.
- Bray RS, Ashford RW, Bray MA. (1973). The parasite causing cutaneous leishmaniasis in Ethiopia. Trans R Soc Trop Med Hyg. 1973;67(3):345-8
- Awad R, Al Rahman Omer A, Abu Shahla N. (2001). A critical review
 of the infectious diseases surveillance system in the Gaza Strip. East
 Mediterr Health J. Jan-Mar;7(1-2):274-9.
- Wilson SM. (1995). DNA-based methods in the detection of Leishmania parasites: field applications and practicalities. Ann Trop Med Parasitol. 1995 Dec;89 Suppl 1:95-100.
- Norton SA, Frankenburg S, Klaus SN. (1992). Cutaneous leishmaniasis
 acquired during military service in the Middle East. Arch
 Dermatol. Jan;128(1):83-7.
- Hepburn NC. (2000). Cutaneous leishmaniasis. Clin Exp
 Dermatol. Jul;25(5):363-70.

- Berman JD. (1997). Human leishmaniasis: clinical, diagnostic, and chemotherapeutic developments in the last 10 years.Clin Infect Dis. Apr;24(4):684-703.
- Kroeger A, Avila EV, Morison L. (2002). Insecticide impregnated curtains to control domestic transmission of cutaneous leishmaniasis in Venezuela: cluster randomised trial.BMJ. 2002 Oct 12;325(7368):810-3.
- Desjeux P. (1999). Global control and Leishmania HIV coinfection.Clin Dermatol. May-Jun;17(3):317-25.
- Postigo JA. (2010). Leishmaniasis in the World Health Organization
 Eastern Mediterranean Region. Int J Antimicrob Agents. Nov;36
 Suppl 1:S62-5. Epub 2010 Aug 21.
- Hotez PJ, Savioli L, Fenwick A. (2012). Neglected tropical diseases of the Middle East and North Africa: review of their prevalence, distribution, and opportunities for control. PLoS Negl Trop Dis. 2012;6(2):e1475
- Schlein Y, Warburg A, Schnur LF, Le Blancq SM, Gunders AE. (1984).
 Leishmaniasis in Israel: reservoir hosts, sandfly vectors and leishmanial strains in the Negev, Central Arava and along the Dead
 Sea. Trans R Soc Trop Med Hyg.; 78(4):480-4.

- Klaus S, Axelrod O, Jonas F, Frankenburg S.(1994). Changing patterns
 of cutaneous leishmaniasis in Israel and neighbouring territories.
 Trans R Soc Trop Med Hyg. 1994 Nov-Dec;88(6):649-50.
- Baneth G, Dank G, Keren-Kornblatt E, Sekeles E, Adini I, Eisenberger CL, Schnur LF, King R, Jaffe CL. (1998). Emergence of visceral leishmaniasis in central Israel. Am J Trop Med Hyg. Nov;59(5):722-5.
- Singer SR, Abramson N, Shoob H, Zaken O, Zentner G, Stein-Zamir C.
 (2008). Ecoepidemiology of cutaneous leishmaniasis outbreak, Israel.
 Emerg Infect Dis. Sep;14(9):1424-6.
- Vinitsky O, Ore L, Habiballa H, Cohen-Dar M. (2010). Geographic and epidemiologic analysis of the cutaneous Leishmaniasis outbreak in northern Israel, 2000-2003. Isr Med Assoc J. Nov;12(11):652-6.

Appendix

استبيان خاص بمرض الليشمانيا الجلدية

عزيزي المواطن إن هذه الاستمارة سوف تستخدم فقط من اجل الدراسة فقط ولن يتم نشر أي أسماء وسوف يكون هنالك سرية تامة وسوف يتم نشر نتائج هذه الدراسة . إن مرض الليشمانيا منتشر في فلسطين وخاصة شمال الضفة الغربية حيث لوحظ في الآونة الأخيرة إن هذا المرض في ازدياد،حيث هذا المرض يسببه طفيل وينتقل إلى الإنسان من خلال بعوضة ال sand fly وهذه البعوضة تتواجد بكثرة في فلسطين، حيث ينتقل الطفيل الى أحشاء البعوضة وذلك بعد لدغ الحيوان الخازن لهذا الطفيل مثل الكلاب الضالة و الوبر الصخري ،وبعد فترة من الزمن تظهر اثار هذه اللدغة اما بشكل حبة او قرحة .ان هذا المرض ليس بخطير و يمكن الشفاء منه و يوجد علاج متوفر في

وزارة الصحة ويعطى مجانا .
المحافظة:
سنة الإصابة:
تاريخ بداية الأعراض
تاريخ التبليغ
الاسم:اسم رب الأسرة
هاتفهات
مكان السكن:
1 – مدينة: أ- في وسط المدينة ب- في الأطراف
2 - قرية: أ- في وسط القرية ب- في الأطراف
3–مخيم
4- في الخلاء (البادية)
العمر:ا
الجنس: 1- ذكر 2-انثى
الوظيفة: الحالة الاجتماعية:
مكان العمل أو المدرسة
سنوات التعليم: المصاب الأب الأم

		ب ؟	بالمرض	ب انتقل لمنطقة فيها إصابات	هل المصا		
					1- نعم		
					√ −2		
••••		• • • • • • • • • • • • • • • • • • • •	•••••	جواب نعم، اذكر المكان:	إذا كان اا		
	· - هل التشخيص مبنى على الأعراض؟						
				1− نعم 🗆			
				□ ⅓ - 2			
	- هل تم تأكيد التشخيص مخبرياً ؟						
	1− نعم						
	□ ⅓ - 2						
				مابة	مكان الإِص		
				4	1- الوج		
				راف	2- الأط		
				ى	3- أخرو		
				الإصابات (عدد الحبات)	اذكر عدد		
				حدة	1- وا.		
				تين	2- اثد		
			• • •	كثر (كم عددها)	1-3		
ماهي طبيعة الإصابة							
	1 –قرحة □						
	2 حبة −2						
				هري للعائلة :	الدخل الشر		
ريباً	دينار أردني تق		•••••	دل الدخل الشهري للعائلة ؟	ما هو مع		
			<u>منزل</u>	وإنات والدواجن القريبة من ال	تربية الحي		
1. حسب الجدول التالي حدد أنواع وأعداد الحيوانات التي يمتلكها صاحب المنزل أو الجيران ؟							
	فترة وجودها	المسافة عن المنزل	العدد	النوع			
				1. أبقار			
				2. ماعز	-		
				3. أغنام (نعاج و خراف)			

4. دجاج

الاصحاح البيئي والصحة الشخصية

الاصحاح البيبي والصحه الشحصيه
1. هل النفايات الصلبة متراكمة حول المنزل؟
1. نعم بشكل واضبح
2. نعم بكميات قليلة
¥.3
2. ما هي طريقة حفظ النفايات
3. ما هي طريقة نقل النفايات؟
بمعدلمرة / الاسبوع
4. ما هي طريقة التخلص النهائي من النفايات
5. ما هي الطريقة المتبعة للتخلص من الحيوانات الميته
6. ما هو معدل وجود جثث حيوانات ميتة قبل الاصابة قرب المنزل؟
1. باستمرار
2. أحياناً
3. نادراً
7. هل يوجد جحور للفئران حول المنزل أو بالقرب منه؟
1. نعم
¥ .2
8. هل يتم التخلص من المياه العادمة عن طريق رشها حول المنزل ؟
1. نعم وبشكل دائم
2. أحياناً
3. نادراً
4.لا مطلقاً
9-هل يوجد على شبابيك المنزل منخل (شبك)
1- نعم
¥-2
3 – البعض
10-هل دائماً تحكم اغلاق منخل النوافذ:
1-نعم دائماً
2-في بعض الاحيان

3- نادراً جداً

11-هل سبق و نمت خارج المنزل او على الاسطح او في الخلاء:

1-نعم في معظم الاحيان

2-نعم احيانا

3-نادرا جداً

¥−4

استخدام المبيدات لمكافحة الحشرات:

1 - هل تستعملون أي من مواد مكافحة الحشرات في المنزل:

1–نعم دائماً

2-نعم احيانا

¥−3

2-هل تستعملون الناموسية اثناء النوم:

1- نعم دائماً

2- احياناً

¥ −3

3-قبل ظهور أعراض المرض هل كان ينام أحد مع المصاب في نفس الغرفة:

1-نعم (حدد الاسماء).....

¥-2

4-هل أصيب أحد من الأشخاص الذين يسكنون بالمنزل بمرض اللشمانيا الجلدية منذ أن سكنتم المنزل وحتى الآن ؟

1-نعم

 $\sqrt{2}$

5-سبق و أن أصيب أحد من الأشخاص الذين يسكنون بالجوار بمرض اللشمانيا الجلدية ؟

1-نعم

¥-2

6. تضاريس المنطقة التي يقع فيها مكان السكن:

أ. منطقة جبلية على قمة الجبل

ب. منطقة جبلية في الوادي

ج. منطقة سهلية

7. وجود كهوف و تصدعات صخرية قريبة من المنزل:

۱. كتيرة و منتشرة
ب. قليلة و متباعدة
ج. غير موجودة
8. هل قام المجلس المحلي برش المنزل بالمبيدات لمكافحة الحشرات خلال فصل الصيف
الذي سبق ظهور المرض ؟
1. نعم (انتقل الى سؤال رقم 9)
¥. 2
3 لا اعرف
9. كم مرة تم رش المبيدات و متى و أين تم رشها، مثلاً: على الجدران داخل المنزل، على
الجدران خارج المنزل داخل الحظائر ؟
1– مرة
3 – مرتان
4- ثلاث مرات
4 - لا اعرف
قسم خاص بالكلاب و الحيوانات البرية:
أ. الفئران والقوارض:
1. هل يوجد فئران أو جرذان حول المنزل أو في الجوار:
أ. نعم
ب. لا
ج. لا أعرف
2. إذا كانت الاجابة على السؤال السابق نعم أين توجد الفئران أو الجرذان يمكن اختيار أكثر من
إجابة؟
أ. داخل المنزل
ب. حول المنزل
ج. قريباً من المنزل في (صِف المكان)متر
د. داخل حظيرة الحيوانات على بعدمتر من المنزل.
ه. أخرى حدد على بعد متر من المنزل.

3. هل يمكن ملاحظة جحور الفئران و أماكن تواجدها حول المنزل و في الجوار؟

أ. نعم

ب. لا

ج. لا أعرف

4. هل سبق و أن رأيت الفئران أو الجرذان أثناء النهار ؟

أ. نعم

ب. لا

ج. لا أعرف

5. هل كانت تظهر الفئران أو الجرذان أثناء النهار بشكل

أ. مستمر يومياً

ب. بين الحين و الآخر

ج. نادراً

ب. الكلاب الضالة:

1. كم تقدر أعداد الكلاب الضالة التي قد تتواجد حول المنزل أو في الجوار:

أ. أكثر من 6 كلاب

ب. من 3 - 5 كلاب

ج. من 1 – 2 كلب

د. غير موجودة

ه. لا أعرف

2. معدل وجود الكلاب الضالة:

أ. باستمرار (يومياً تقريباً)

ب. من 3 - 4 أيام / اسبوع

ج. مرة اسبوعياً

د. مرة /شهر

ه. نادراً

3. بعد أماكن تواجدها عن المنزل:

أ. أقل من 100 متر

ب. من 100 – 300 متر

ج. أكثر من 300 متر

4. أوقات توجدها:

أ. أثناء ساعات المساء

ب. أثناء النهار

ج. أثناء ساعات المساء أو النهار

د.على مدار الساعة

5. فترة تواجدها:

أ. دقائق معدودة (تمر من المنطقة)

ب. من 1-3 ساعة

ج. أكثر من ثلاث ساعات

د. الكلاب المنزلية:

- 1. هل كان يوجد في المنزل أو الجوار (على بعد 300 متر) كلب أو عدة كلاب قبل ظهور الصابة بمرض اللشمانيا ؟ (السؤال حول الظروف في فترة ظهور الاصابة)
 - 1. نعم
 - צ. צ

وسام صبيحات 0599281212

جامعة النجاح الوطنية كلية الدراسات العليا

وبائية داء الليشمانيا الجلدية في شمال الضفة الغربية-فلسطين

إعداد وسام صبيحات

إشراف د. أيمن حسين

قدمت هذه الأطروحة استكمالاً لمتطلبات درجة الماجستير في الصحة العامة بكلية الدراسات العليا في جامعة النجاح الوطنية في نابلس – فلسطين.

ب

وبائية داء الليشمانيا الجلدية في شمال الضفة الغربية-فلسطين إعداد

وسام صبيحات إشراف

د. أيمن حسين

الملخص

لقد كانت الليشمانيا مشكلة صحية عامة في جنوب غرب آسيا والعالم العربي منذ الأزل وذكرت أيام حكم الفراعنة في مصر والأشوريون في بلاد ما بين النهرين. والسبب لهذا المرض طفيليات الليشمانيا. هناك عدة أنواع من هذه الطغيليات التي تسبب داء الليشمانيا حيث أكد الأشكال الثلاثة: الجلدي (MCL ، CL) والحشوية (VL) داء الليشمانيا.ان شمال فلسطين هي مركز لمنطقة تعيش فيها CL البسيطة هي مفرطة التوطن. ان طفيلي الليشمانيا ينتقل عن طريق ذبابة الرمل الناقل بدعم من مجموعة واسعة من الحيوانات الخازنة موزعة على معظم المناطق المأهولة في فلسطين هنالك نوعان من داء الليشمانيا في فلسطين : واحد هو CL الرئيسية الناجمة .L. major or L tropica. والآخر هو الحشوية الناجم عن الطفيلية L. infantum وتفيد التقارير الرسمية أن معدل حدوث داء الليشمانيا في العام2003 في جميع المناطق الفلسطينية في الضفة الغربية باستثناء قطاع غزة أكثر من 10 لكل 100000 الأهداف: وبائية مرض الليشمانيا الجلدية في فلسطين والدول المجاورة ويبدو أنه يمر بمرحلة انتقالية. من ملاحظتنا أثناء العمل في عيادة الأمراض المعدية في وزارة الصحة ، لاحظنا ارتفاعا في عدد المرضى الذين يعانون من الليشمانيا الجلدية في منطقة شمال الضفة الغربية. ولذلك، تم تصميم هذه الدراسة لدراسة حالات الليشمانيا الجلدية خلل فترة السنوات العشر السابقة ، فضلا عن دراسة بيئية، والعوامل الوبائية والاجتماعية التي يمكن أن تؤدي إلى هذا الارتفاع. المنهجية: هذه الدراسة هي بأثر رجعي مستعرضة الدراسة. تم استعراض 1150 ملفات المرضى من أجل ملء استبيان صمم من قبل الباحث. يتضمن الاستبيان الديمغرافية، والأسئلة السريرية والتشخيصية، والوبائية. تم جمع معلومات عن العمر والجنس والإقامة والمعلومات الشخصية وكذلك معلومات عن الحيوانات المستأنسة

والبرية حول المرضى. وإنه أيضا تم جمع معلومات عن طبيعة المنازل والتدابير الوقائية التي تم اتخاذها من قبل الناس لتجنب لدغة ذبابة الرمل الناقل. النتائج: إن النتائج الأكثر إثارة للدهشة وجدت في هذه الدراسة أن الدراسة تؤكد أن المنطقة مفرطة التوطن لداء الليشمانيا الجلدية . وتبين أن نسبة الإصابة في منطقة طوباس وجنين أكثر من باقي المناطق في هذه الدراسة بما لا نقل عن 5-10. لا يوجد فرق بين الذكور والإناث في الإصابة الليشمانيا الجلدية . ومع ذلك، وجد أن فئة الأطفال هي الأكثر عرضة. وأظهرت موقع الإصابة بين المرضى التي تتأثر في الغالب الأطراف والساقين. ولم يبلغ عن الفئران والكلاب من قبل المرضى حول منازلهم. ومن المعروف أن الأطراف والساقين. ولم يبلغ عن الفئران والكلاب من قبل المرضى حول منازلهم. ومن المعروف أن تلك الحيوانات تعمل كمخازن للناقلات ذبابة الرمل. تم العثور على أكثر من 70٪ من المرضى CL سكان الضواحي، رغم أنه تبين أن المرضى من مواقع جغرافية مختلفة.