Deanship of Graduated Studies

Al-Quds University

Environmental and Social Determinants and Risk Factors for Cutaneous Leishmaniasis: A Case- Control Study in Hebron and Bethlehem Governorates

Maram Hassan Hamza Almakharzeh

M.Sc. Thesis

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Thesis Approval

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1446/2024

Dedication

اهداء

بسم الله الرحمن الرحيم

قال تعالى ﴿وَقُل رَّبِّ زِدْنِي عِلْمًا﴾

الحمد لله على عطائه، الحمد لله على رزقه، الحمد لله على آلائه، الحمد لله على نعمائه، الحمد لله حمد الشاكرين والشكر لله شكر الحامدين.

اللهم صلِّ على سيدنا محمد طب القلوب ودوائها، وعافية الابدان وشفائها، ونور الابصار وضيائها، وعلى آله وصحبه وسلم.

الى غزة العزة الى شهدائنا الابرار لشعبنا الصامد فوق التراب وسط الانقاض للام الفاقدة المفقودة لأطفال غزة العزة

الى امي جنة الدنيا والاخرة الى ابي الجبل الصامد الي اخوتي ونور قلبي

الى عائلتي الصغير الكبيرة زوجي العزيز (الدكتور هارون مسودة)، ابنائي فلذات كبدي

الى الذين كانوا رمز العلم الى القدوة الرفيعة المستوى الى الانسانية المتواضعة الي جميع اساتذتي جميعا دون استثناء كل الشكر والاحترام.

واخص بالذكر (الاستاذ الدكتور ياسر عيسى)

الذي تفضل بالإشراف على هذا البحث فجزاه الله عنا كل خير.

له كل التقدير والاحترام.

الى كل من ساندني وشجعني وساعدني من اقارب واصدقاء.

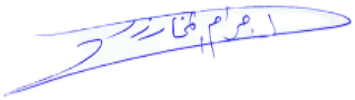
كل الشكر والاحترام

مرام حسن المخارزة

Declaration

I hereby declare that this thesis submitted for the degree of master is entirely of my own work and research, neither this thesis nor any part of it has been submitted to any degree in higher education Universities or institutions.

Maram Hassan Almakharzeh



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Maram Hassan Almakharzeh

2024

Abstract

Background: Cutaneous leishmaniasis is a persistent public health challenge in Palestine, particularly within the Hebron and Bethlehem governorates. This study aims to analyze the epidemiological characteristics of cutaneous leishmaniasis (CL) cases by person, place, and time in Hebron and Bethlehem Districts. It seeks to identify the sociodemographic and environmental risk factors associated with CL transmission in these endemic areas through statistical analysis. Additionally, it assesses the relationship between climate factors, particularly rainfall, and CL occurrence over recent years. Finally, the study evaluates the effectiveness of recent preventive measures implemented by municipalities and health authorities in these districts to combat the disease.

Methods: A case-control study was conducted with 207 confirmed cases of cutaneous leishmaniasis and 414 controls (1:2 ratio) matched by age, sex, and residential area. Data were gathered through structured interviews and validated questionnaires covering socioeconomic status, housing conditions, environmental exposures, and behavioral factors. Statistical analyses, including chi-square tests, t-tests, and multivariate logistic regression, were used to identify significant risk factors.

Results: The spatial distribution of cases revealed that 29.9% were concentrated in Zatara, A'rab ar Rashayida, and Al-dirat, with notable clusters in Wadi Araba, Dimona, Beer Sheba, and Eilat (16.4%), as well as Massafer Bani Na'im (14.5%). Multivariate logistic regression identified several key risk factors for cutaneous leishmaniasis. Household crowding was a significant predictor, with those in overcrowded conditions showing increased odds of infection (OR = 2.10, 95% CI: 1.45–3.05). Poor housing quality, characterized by inadequate sanitation and proximity to areas with high vector activity, further elevated the risk (OR = 2.35, 95% CI: 1.50–3.70). Lower socioeconomic status was strongly associated with higher incidence rates, disproportionately affecting individuals in the lowest income brackets ($p < 0.05$).

Environmental factors, including rainfall and topography, were also significant. The study found that areas with lower annual rainfall (<300 mm) had a higher incidence of cutaneous leishmaniasis, possibly due to the drier conditions favoring the breeding and survival of sandfly vectors ($p < 0.05$). Topographical analysis revealed that cases were more common in low-lying areas and valleys, which provide suitable microhabitats for sandflies. These areas often have higher humidity levels and vegetation, which can support vector proliferation and increase human exposure risk (OR = 1.90, 95% CI: 1.30–2.80).

Behavioral factors, particularly outdoor sleeping habits and insufficient use of protective measures during peak vector activity at night, were significantly correlated with higher infection rates ($p < 0.01$). Proximity to animal shelters and unprotected agricultural areas increased the likelihood of exposure to sandfly bites, the primary vector for leishmaniasis (OR = 1.85, 95% CI: 1.20–2.85). Educational programs aimed at improving knowledge and practices related to vector protection showed potential as an intervention, indicating that public awareness is critical in mitigating the spread of the disease.

Conclusions: The findings underscore the importance of improving socio-economic conditions, enhancing housing and environmental sanitation, and promoting awareness about leishmaniasis to mitigate the disease's spread. Targeted interventions, including the use of insecticide-treated

bed nets and better waste management, are recommended to reduce infection rates. Continued surveillance and specific and tailored public health strategies are essential to address the ongoing challenge of leishmaniasis in Palestine.

Keywords: Leishmaniasis, case-control study, environmental determinants, social determinants, Palestine, Hebron, Bethlehem, public health, epidemiology

Contents

List of tables

List of figures

List of appendices

Abbreviations

AOR	Adjusted Odds Ratio
CanL	Canine Leishmaniasis
CDC	Centers for Disease Control and Prevention
CI	Confidence Intervals
CL	Cutaneous leishmaniasis
EMR	Eastern Mediterranean Region
GAM	Generalized Additive Models
HIV	Human Immunodeficiency Virus
LAmB	liposomal amphotericin B
LCL	localized cutaneous leishmaniasis
LD	L. *donovani*
LI	L. *infantum*
ML	Mucosal leishmaniasis
MOH	Ministry of Health
NTD	Neglected Tropical Disease
NWCL	New World CL
OR	Odds Ratio
OWCL	Old World CL
PAHO	Pan American Health Organization
PCBS	Palestinian Central Bureau of statistics
VL	Visceral leishmaniasis
WHO	World Health Organization
ZCL	Zoonotic Cutaneous Leishmaniasis

CHAPTER ONE: BACKGROUND

1.1 Introduction

Leishmaniasis, a neglected tropical disease, poses a significant global health challenge, particularly in regions where poverty and climate conditions promote its transmission. The disease is caused by various species of protozoa, such as Lutzomyia, Psychodopygus, and Phlebotomus, transmitted primarily through the bites of infected female sandflies. These small, nocturnal insects are typically found in animal burrows, woodlands, and cracks in mud and stone walls, biting between dusk and dawn, often unnoticed. The epidemiology of leishmaniasis is closely linked to socio-ecological determinants, including poverty, and is influenced by social, environmental, and climatic factors (WHO, 2022; Jeronimo *et al.*, 2011). Clinically, leishmaniasis manifests in three main forms: cutaneous, mucocutaneous, and visceral.

Leishmaniasis is endemic in several regions globally, including Africa, the Middle East, South Asia, Southern and Northern Europe, South America, and Central America. However, its distribution is expanding to non-endemic areas due to increased international travel (Eiras *et al.*, 2015). The World Health Organization (WHO) reports that leishmaniasis has been documented in 102 countries, with cutaneous leishmaniasis present in 48 countries (WHO, 2018). Annually, approximately 350 million people are at risk, with over 14 million currently infected and more than 2 million new cases reported worldwide (WHO, 2007).

Multiple cofactors contribute to the spread of leishmaniasis, including physical and biological factors, biodiversity, socioeconomic conditions, environmental changes, deforestation linked to urbanization, the presence of domestic animals, and standards of living (Oliveira *et al.*, 2021; Singh, 2019). Human activities that alter topography play a critical role in the spread of cutaneous leishmaniasis (CL). These activities disrupt the ecological balance, creating new environments—such as forests, rural areas, peri-domestic settings, and urban zones—that are conducive to the survival of various vector species adapted to these changes (Shaw, 2007; Lainson & Shaw, 1978). Research indicates that large-scale infrastructure projects, including hydroelectric facilities, dams, roadways, railways, and rural colonization efforts, significantly facilitate CL transmission by drastically altering local environmental conditions (Lainson & Shaw, 1978; Shaw, 2007; WHO, 2010).

In Palestine, the incidence rates of cutaneous leishmaniasis (CL) were reported as 1.16 cases per 100,000 population, and 2.02 cases per 100,000 in the West Bank, while visceral leishmaniasis (VL) rates were 0.02 cases per 100,000 in Palestine and 0.04 cases per 100,000 in the West Bank. Over the past seven years, both CL and VL incidences in Palestine have fluctuated, showing a general declining trend (Ministry of Health [MOH], 2022). CL infections in the West Bank accounted for approximately 1.9% of all parasitic infections in Palestine, with *Leishmania tropica and Leishmania major* as the primary causative agents. Between 2008 and 2017, 2,672 CL cases and 40 VL cases were reported in the West Bank, with the highest CL prevalence in Jericho (603 cases), Tubas (503), Jenin (462), Hebron (228), and Bethlehem (191) (Ministry of Health, Environmental Health Department, 2023, personal communication). The West Bank is home to three Leishmania species—*L. tropica*, *L. major*, and *L. infantum*—which

cause both CL and VL, with VL predominantly affecting villages in the western areas near Israeli VL endemic regions; no data is available for the Gaza Strip (Amro *et al*., 2009).

Data on CL caused by *L. tropica* in Palestine is limited. However, reports indicate that leishmaniasis has been documented in all Palestinian districts, with an incidence rate exceeding 10 per 100,000 in the West Bank in 2003 (Ministry of Health-PHIC, 2004). The incidence of the disease increased from 0.13 per 100,000 in 1999 to 9.7 per 100,000 in 2003, with a similar rate of 9.7 per 100,000 observed from 2004 to 2005. The highest incidence was recorded in the Tiberias district at 62.5 per 100,000. Between 2002 and 2009, several CL cases caused by *L. tropica* were reported in West Bank districts, with an annual incidence rate of 23.0 per 100,000 (Azmi *et al*., 2017). The Palestinian Ministry of Health recorded three significant leishmaniasis outbreaks: in 1996 (150 cases), 2004 (over 250 cases), and 2015 (380 cases). It is estimated that 340 VL cases occurred among the Palestinian population between 1990 and 2017, excluding Gaza due to data limitations, with an annual incidence rate of 0.73 cases per 100,000 population (MOH, 2022).

Leishmaniasis, comprising both cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL), is an ongoing public health challenge in Palestine, with significant variability in its distribution and impact across different regions. Over the past three decades, multiple studies have documented the epidemiological characteristics, spatiotemporal patterns, and future projections of leishmaniasis in Palestine. CL has been particularly prevalent in areas such as Jenin, Jericho, and Tubas, with over 5,800 cases reported between 1990 and 2020. The disease is primarily caused by *Leishmania tropica* and *Leishmania major*, with *Phlebotomus sergenti* identified as the main vector in these regions. Future projections suggest an increase in CL incidence in the northwestern West Bank and the possible emergence of new endemic foci in the Gaza Strip due to climate change.

In contrast, VL has a more localized distribution, predominantly affecting young children in the Hebron district and the western parts of the West Bank. Studies have identified *Leishmania infantum* as the causative agent, with *Phlebotomus syriacus* and *Phlebotomus tobbi* as potential vectors. Despite fluctuations in incidence, VL continues to be a concern, with projections indicating that certain areas may remain at risk in the future. Additionally, parasitic infections, including leishmaniasis, have shown differing patterns between the West Bank and Gaza Strip, with Gaza recording a higher overall burden. These findings highlight the need for ongoing surveillance, effective vector control measures, and public health education to mitigate the spread of leishmaniasis and reduce its burden on the Palestinian population (Amro *et al*. (2022); Amro *et al.,* (2020); Hamarsheh and Amro (2020); Azmi *et al.* (2012); Al-Jawabreh *et al.* (2004); Amro *et al.* (2009)).

1.2 Problem Statement

In Palestine, as noted by Amro *et al*. (2022), the disease has emerged as a major public health concern, particularly in the West Bank, with the majority of cases being transmitted by infected *Phlebotomine* sandflies. Due to lacking data from Gaza, WHO recommended for deep research to investigate the incidence, prevalence, and dispersion of CL in Palestine despite CL cases were registered in Sinai Peninsula (WHO, 2021).

Groups of factors, including climatic, socioeconomic, and ecological settings, can contribute in development of leishmaniasis. Potential risk elements for leishmaniasis including substandard living conditions, low educational attainment, disorderly surroundings and environment, and limited awareness have been investigated by numerous studies (Valero & Uriarte, 2020; Ullah *et al*., 2016; Terefe *et al*., 2015; Singh, 2019; Salah *et al*., 2016; Picado *et al*., 2014; Oryan & Akbari, 2016; Mandal *et al*., 2020; Maia *et al*., 2016). To the researchers' knowledge, these factors had not been investigated in this area before. Lower incidence of cutaneous leishmaniasis (CL) was found to be significantly linked to the higher educational attainment of the head of household, and children sleep under bed nets were found in a study conducted aimed to investigate the sero-prevalence of leishmania major and the risk factors associated with contracting the disease in Jericho city and nearby Aqbat-Jaber refugee camp (al Jawabreh *et al.*, 2003).

Leishmaniasis is a disease that is endemic and mostly it was spread in Jericho city due to its geographical and climatic features, which is suitable for the sand fly, the vector for this disease, to survive. The incidence of disease increased in most parts of Palestine including cold areas, which could be due to the climatic changes that occurred in Palestine mainly during the last ten years (Ministry of Health-PHIC, 2004). It seems that Leishmaniasis distributed all over the districts in Palestine and became not limited to Jericho and warm region. So, this study will try to answer the main research question: ***What are the main risk factors associated with Cutaneous leishmaniasis in Hebron and Bethlehem Districts- Palestine?***

1.3 Justification of the study

Leishmaniasis, a parasitic disease, presents a significant social and medical threat across approximately 99 countries worldwide (Alvar *et al.*, 2012; Álvarez-Hernández *et al.*, 2020; de Souza *et al.*, 2018). Globally, the prevalence of leishmaniasis in all its forms is estimated at 12 million cases, with about 1.5 to 2 million new cases of cutaneous leishmaniasis (CL) and 500,000 new cases of visceral leishmaniasis (VL) annually. This disease is responsible for around 50,000 deaths each year, making it the second deadliest parasitic disease after malaria (Desjeux, 2004; Oryan *et al.*, 2007; WHO, 2002).

Leishmaniasis has recently re-emerged in various regions, intensifying global health and economic concerns due to its vector-borne nature. The epidemiology of leishmaniasis is influenced by the interactions between hosts, reservoirs, vectors (human, animal, and sandfly), and environmental factors. The emergence and spread of leishmaniasis can be attributed to numerous changes in environmental and ecological factors, including weather patterns, water catchment, irrigation, deforestation, climatic fluctuations, immunosuppression from organ transplants or HIV, emerging drug resistance, increased human movement to endemic areas, and domestic dog ownership.

There remains a limited understanding of the environmental and social determinants that explain why some individuals contract the disease while others do not (Sbehat, 2012). Research on leishmaniasis has primarily focused on isolated or limited factors and has been conducted predominantly in regions where Leishmania is prevalent. Consequently, there is an urgent need

for comprehensive investigations into the clinical, environmental, co-infection, and resistance factors associated with Leishmania in endemic areas. Despite its wider geographical distribution compared to the past, leishmaniasis continues to be one of the world's most neglected diseases, disproportionately affecting impoverished and developing regions.

From the researcher's experience and observations in the preventive medicine department, data indicate that some individuals within the same household contract the infection while others do not. This observation raises critical questions about the underlying factors contributing to this variability. The findings from this study will help clarify the dynamics of the disease. Understanding the risk factors that affect both humans and animals is crucial for gaining insights into disease transmission and for developing effective public health and control measures (Salah *et al.*, 2016).

Given the increasing incidence of leishmaniasis in Palestine, it is imperative to prioritize health education and raise awareness among the population about the associated risk factors. To address this effectively, it is essential to identify the specific risk factors for leishmaniasis within the communities residing in the affected areas.

The coexistence of different *Leishmania* species and their association with specific geographic areas further highlights the need to understand the environmental and social factors influencing disease occurrence and spread. Investigating these determinants is crucial for developing tailored prevention and control strategies to meet the unique needs of different regions in Palestine. The ultimate goal of this study is to propose recommendations that improve health outcomes and reduce the burden of the disease in affected areas.

1.4 Research Question

What are the potential environmental and sociodemographic determinants that can independently pose a risk for Leishmaniasis in the Hebron and Bethlehem Districts of the West Bank, Palestine?

1.5 Objectives of the study

The study aimed to address the primary research question by examining the key determinants of leishmaniasis among Palestinians, specifically in the southern part of the West Bank (Hebron and Bethlehem Districts). The specific objectives are as follows:

1. To analyze the characteristics of leishmaniasis cases by person, place, and time in the Hebron and Bethlehem Districts. This will involve collecting and evaluating epidemiological data on demographic, geographic, and temporal patterns of the disease over time.
2. To identify the sociodemographic and environmental risk factors associated with leishmaniasis transmission in these endemic areas. This objective will be achieved by conducting statistical analysis of risk factors.
3. To assess the relation between climate (rainfall) and Cl occurrence during last years.

4. To assess the latest preventive measures implemented by municipalities and health directorates in the two governorates to combat this disease.

1.6 Main hypothesis

This study proposes that there is a relationship between environmental and socio-demographic factors and the occurrence of leishmaniasis among Palestinians living in the Hebron and Bethlehem Districts in Palestine.

Also, the study hypnotized that increased levels of annual rainfall are positively associated with the occurrence of leishmaniasis in endemic areas.

1.7 Thesis structure

This thesis consists of the following chapters:

Chapter One: Background part of the thesis including introduction, problem statement, justification, aims of the study, and the research questions.

Chapter Two: Literature review which provides an overview of literature concerning leishmaniasis, encompassing its epidemiology, pathogenesis, clinical presentations, diagnostic techniques, treatment options, and preventive measures. It synthesizes existing research to contextualize our study and pinpoint areas where knowledge gaps exist.

Chapter Three: Methodology: this chapter describes the research design, study area, study population, sampling techniques, ethical considerations, data collection methods, and statistical analyses used in the study.

Chapter Four: Results: this chapter presents the results of our study in a clear and organized manner. It includes descriptive statistics, tables, figures, and any other relevant data representations.

Chapter Five: includes the discussion of the results, limitations and strengths of the study, conclusion, and recommendations.

In addition to references and appendices

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

The leishmaniasis could occurred after being bitten by a female sandfly. Recently, it became a health concern in many countries worldwide (tropical, subtropical, and southern Europe). The natural environments vary from deserts to rain forests. Leishmaniasis usually has greater prevalence rates in countryside or rural than in urban environments, while cases have been reported in several city suburbs. Alterations in climate and environment can play a significant contribution in the geographical expansion of sand fly vectors, thereby expanding the endemic regions. The spreading and transmission of the disease may be influenced by such alterations to climatic patterns and environmental factors (CDC, 2020).

According to current estimates, diseases carried by arthropod vectors, or vector-borne diseases account for 17% of all infections leading to at least 700,000 fatalities annually due to its high incidence, morbidity, and mortality. Neglected Tropical Diseases (NTDs) are diseases that affect people disproportionately in tropical and subtropical economically disadvantaged countries (Cecílio *et al.,* 2022; Álvarez-Hernández *et al.,* 2020; Herricks *et al.,* 2017). Leishmaniasis encompasses a collection of illnesses triggered by 20 distinct species of leishmania which are spread by various species of phlebotomine sand flies. Even after extensive research efforts, several aspects of leishmaniasis are still unclear. For example, distinct *leishmania* species are associated with comparable clinical presentations, *L. infantum* can cause both CL and VL. These observations highlight the complex nature of leishmaniasis by suggesting that factors other than parasite tropism and virulence may affect the disease's occurrence. It poses a considerable burden on public health due to its wide distribution and diverse clinical manifestations. The transmission of Leishmania parasites occurs primarily after the bite of infected sand flies, making it crucial to understand the epidemiology, pathogenesis, and factors influencing the spread of the disease (CDC, 2020). A protozoa parasite from more than 20 leishmaniasis species is the cause of leishmaniasis. Based on the reservoir hosts, leishmaniasis was divided into two major categories: zoonotic (for wild and domestic animals) and anthroponotic (where the main source is humans) (Mokhtar I, Mosa B, Abdallah M., (2017); Talari S, *et al.,* 2010). In regard to human leishmaniasis, CL is considered the most prevalent type (Hawash YA, *et al.,* (2018); El-Beshbishy HA, *et al.,* (2013)).

L. tropica has also been claimed to be endemic in Israel and the Philistines, while the cycle of transmission is not completely understood. With a widespread geographic distribution throughout the region, Phlebotomus (Paraphlebotomus) sergenti has been identified as the primary vector of *L. tropica*. *Phlebotomus arabicus* and *Phlebotomus similis* have also been documented. *Leishmania major* has reportedly been linked to CL in Southern Israel; this type of the illness is self-healing but makes the patient anxious. The reservoir host is the obese sand rat *Psammomys obesus* (Cricetidae: Gerbillinae), and *P. obesus* and the sand fly *Phlebotomus papatasi* (Diptera: Psychodidae) serve as the vectors. *L. majori*, the parasite that causes CL and VL, is the primary carrier of both the disease and its primary vector, *P. papatasi.* VL is primarily brought on by *L.infantum*, though *L. tropica* can also be to blame in some cases. CL comes in two forms: ZCL and ACL, which are caused by *L. major* and *L. tropica*, respectively. Rodents

are the main reservoir hosts, and some of the more endemic species include Rhombomys (R.) opimus, Meriones libycus, Tatera (T.) indica, and Meriones hurrianae. Phlebotomus papatasi transmits *L. major*, whereas Phlebotomus sergenti transmits *L. tropica* (Wasserberg G, et al., (2013); Kyari, S. (2024)). There are around 90 kinds of sandflies that can spread leishmania parasites (WHO, 2023). Table 2.1 shows the 20 leishmaniasis parasites (Kyari, S. (2024))

Table 2.1: Parasites species and clinical form of leishmaniasis and their geographical distribution

Clinical forms	**Leishmania parasite**	**Geographical distribution**
CL	*L. major*, *L. tropica*, *L. infantum*, and *Labrus donovani; L. braziliensis*: *Lutzomyia neivai*, *Lu. Whitmani*, *L. Cortelezzii complex* (*L. Cortelezzii–L. Sallesi*), *L. Migonei*, and *L. Pessoai*, *L. (L.) peruviana, L. lainsoni*, *L. amazonensis*, *L. infantum chagasi*, *L. Mexicana*, *Leptodactylus colombiensis* and *L. equatoriensis*	Morocco, Algeria, Tunisia, Libya, Egypt; Chad; Sudan, South Sudan, Ethiopia, Kenya, Uganda and Somalia; Niger, Nigeria, Senegal and Mali; Cameroon, Burkina Faso, Mauritania, Gambia and Guinea, Ghana; Syria, Lebanon, Israel, Palestine, Iran, Saudi Arabia, Iraq, Pakistan, Afghanistan, Turkmenistan; Greece; United State of America; Bolivia, Brazil, Colombia, Peru; Sri Lanka, China, Nepal Bangladish; India, and
MCL	*L. viannia braziliensis, L. viannia amazonesis, L. viannia panamensi*s and *L viannia guyanesis*	Senegal; Colombia; Sri Lanka
DCL	*L. Mexicana, L. aethiopica, L. amazonensis, L. pifanoi, L. guyanensis*, and *L. panamensis*	Mexico, United States, and Canada
VL	*L. donovani, L. infantum, L. tropica, L. chagasi*	Ethiopia, Kenya, Somalia, South Sudan, Sudan, Chad, Togo, Burkina Faso, Cameroon and Uganda; Iran, Bangladesh, Sri Lanka and Nepal; India; Brazil, Argentina, Colombia; India

2.2 Literature Review

2.2.1. Leishmaniasis Classifications:

There are different forms of leishmaniasis (CDC, 2020):

2.2.1.1. Visceral leishmaniasis (VL) or kala-azar:

Over 95% of untreated cases of kala-azar, the most serious type of leishmaniasis, resulted in death. Patients with this condition typically experience fevers, weight loss, spleen and liver enlargement, and anemia. With 50,000 to 90,000 new cases worldwide each year, the majority of cases are in Brazil, East Africa, and India; only 25–45% of these cases are reported to the WHO. VL is endemic to Iraq, Somalia, Sudan, Palestine, and Yemen; it mostly affects poor populations and carries a high risk of outbreak and fatality. Malnutrition, becoming homeless, poor housing, compromised immune systems, scarce resources, and environmental alterations

like urbanization and deforestation are all contributing factors (WHO, 2023; Amro, A., and Hamarsheh, O., 2020).

Domestic dogs (Canis familiaris) are the primary disease reservoir in both urban and rural regions, Foxes (Lycalopex vetulus and Cerdocyon thours) and some marsupials (Didelphis spp.) act as reservoirs in the wild. Congenital transmission and needle sharing among drug addicts are two routes of infection. Direct person-to-person transmission does not occur. To prevent human infection, which cannot be averted by a vaccine, it is recommended to stay indoors between dusk and dawn, use mosquito nets, wear protective clothing and apply insect repellents to minimize contact with vectors. Vector control involves integrated environmental sanitation practices, with spraying residual insecticides being a safe and effective methods (PAHO, 2012).

Between 1993 and 2007, 76 cases of visceral leishmaniasis (VL) were reported in the Hebron district of the West Bank, Palestine, all affecting children under 9 years old, with a median age of 2 years. *Leishmania infantum* was identified as the causative agent, and serological surveys indicated an 8.4% seropositivity rate among children, particularly those in households with previous VL cases or domestic animals. The epidemiological pattern of VL in Hebron aligns with typical Mediterranean region trends, and preliminary sandfly surveys identified *Phlebotomus syriacus* and *Phlebotomus tobbi* as potential vectors (Amro *et al.*, 2009). VL continues to be endemic in the West Bank but not the Gaza Strip

2.2.1.2. Cutaneous leishmaniasis (CL):

Cutaneous leishmaniasis (CL) was first described in the Old World by Lewis and Cunningham in 1876. This condition is primarily caused by *L. major* and *L. tropica*, while in the southwestern regions of Mexico and along the Guatemalan border, it is attributed to *Leishmania mexicana*. CL lesions typically develop on areas of the body exposed to sandfly bites, with the most frequently affected sites being the ears (especially the helix and anti-helix), nose, upper lip, cheeks, legs, hands, forearms, and ankles. In Guatemala, the upper limbs are most commonly affected, accounting for up to 43% of cases. The incubation period ranges from 1 to 4 weeks but can extend to several years. Patients often have a history of travel to endemic areas. In the New World, CL is a zoonosis caused by at least ten species of *Leishmania*, primarily within the *mexicana* and *braziliensis* complexes (Dedet, 1999).

The most prevalent type results exposed body areas with skin lesions, especially ulcers, which can cause severe impairment or social stigma in addition to permanent scarring, approximately 95% of cases of cutaneous leishmaniasis (CL) occur in the Middle East, Central Asia, the Americas, and the Mediterranean region, Globally, between 600,000 and 1 million new cases are reported to WHO of which 80% are from Mediterranean region. (WHO, 2023).

This disease can be occurred due to existence of different leishmaniasis species depends on the geographic areas. Each species has its own reservoir host. The main cause of cutaneous leishmaniasis (CL) in the Old World is *L. major*, which is usually spread via rodent reservoirs. The density of vector populations is correlated with the frequency of CL outbreaks. Epidemics of zoonotic cutaneous leishmaniasis (ZCL)have been associated with distinct rodent populations. For instance, ZCL outbreaks in Ethiopia are linked to *L. aethiopica*, but anthroponotic cutaneous leishmaniasis is believed to be caused by *L. tropica* throughout the Middle East and North Africa. But animals like dogs, livestock, and wild species can also

contract the disease and could severe as potential reservoirs for human infection. Several *leishmania* (Viannia) species are found in the New World and cause CL. Several *leishmania* species cause cutaneous leishmaniasis in distinct regions: the Old World (Eastern Hemisphere) and the New World (Western Hemisphere). In the Old World, *L. tropica*, *L. major*, *L. aethiopica*, *L. infantum*, and *L. donovani* are the primary agents. Conversely, in the New World, the *L. mexicana* species complex (*L. mexicana, L. amazonensis, and L. venezuelensis*) and the subgenus Viannia (L. [V.] braziliensis, L. [V.] guyanensis, L. [V.] panamensis, and L. [V.] peruviana) are prevalent, with L. infantum/L. chagasi also contributing to cutaneous leishmaniasis (CDC, 2023).

From 1990 to 2020, Palestine recorded 5,855 cases of cutaneous leishmaniasis (CL), with an average annual incidence rate (AAIR) of 18.5 cases per 100,000 population. The male-to-female ratio was 1.25:1. Patient ages ranged from 2 months to 89 years, with a mean age of 22.5 years, a standard deviation of 18.67 years, and a median age of 18 years. Over 65% of cases were concentrated in three West Bank governorates: Jenin (29%, 1,617 cases), Jericho (25%, 1,403 cases), and Tubas (12%, 658 cases), while no cases were reported in the Gaza Strip. CL incidence typically increases in December and peaks in March and April. Future projections suggest a potential rise in CL cases in the northwestern West Bank, a possible decline in Jericho and Tubas, and the emergence of new endemic areas in the Gaza Strip (Amro *et al.,* 2022).

Sawalha *et al*. (2003) identified five potential Phlebotomus vectors of leishmaniasis in the West Bank. Of these, *P. papatasi* was the most common (approximately 90%), followed by *P. syriacus* (8%), and *P. mascitti* (2%). *P. sergenti and P. tobbi* were less common. They concluded that *P. papatasi, P. sergenti, and P. syriacus* are likely the primary regional vectors for *L. major, L. tropica, and L. infantum*, respectively. In Hebron Governate, *P. syriacus* and *P. tobbi* were present in 45% and 10% of samples, respectively, while in Jenin, *P. tobbi* and *P. syriacus* were found in 15% and 13% of samples, respectively. In northern Palestine, *P. perfiliewi* was found in 45% of samples. These species are considered potential vectors for *L. infantum* in the Mediterranean basin.

2.2.1.3. Mucocutaneous leishmaniasis (MCL):

Mucosal leishmaniasis (ML) develops when cutaneous leishmaniasis (CL) infection extends to mucosal surfaces, leading to symptoms such as nasal congestion, bleeding, and ulcers in the mouth and throat, which can cause facial deformities. ML is predominantly linked to infection with *L. braziliensis* (Glesby *et al.,* 2012). Resulting from partial or complete destruction of mucous membranes in the nose, mouth, and throat. Over 90% of mucocutaneous leishmaniasis cases are reported in Bolivia, Brazil, Ethiopia, and Peru (WHO, 2022). According to WHO (2020), CL is the predominant type and is characterized by skin lesions. People with CL continue to have no symptoms (WHO, 2020). These lesions (one or more) appeared on their bodies, which can change in size and appearance over time. These scores start off as nodules and can develop into ulcers that have a center and a raised border, mimicking a volcanic shape (WHO, 2019).

Each year between 26,000 and 65,000 new cases are expected to occur globally, however, only 19-37% of these cases are formally reported to health authorities, despite an estimated 12 million cases worldwide. Malnutrition, population dislocation, substandard housing, compromised

immune systems, and low socio-economic position are all associated with the disease. In the Eastern Mediterranean Region (EMR), which includes Afghanistan, Iran, Iraq, Pakistan, and Syria, Leishmaniasis has been reported. A total of 70% of CL cases worldwide are accounted for by the EMR alone (Eshetu & Mamo, 2020; WHO, 2022).

In occupied Palestine "Israel" nineteen patients (11.5%) were diagnosed with MCL among the cohort of travelers returning from Latin America with leishmaniasis. Among them the majority (18 patients (95%)) were also males (Solomon, M., *et al.,* 2022).

2.2.2. Leishmaniasis Clinical Presentation:

When an individual is bitten by a sandfly carrying leishmania parasites, cutaneous leishmaniasis (CL) typically develops within weeks, resulting in skin lesions on exposed areas of the body. In New World cutaneous leishmaniasis (NWCL), symptoms often appear as nodules or ulcers, frequently accompanied by local lymphadenopathy. Old World cutaneous leishmaniasis (OWCL) presents with similar symptoms but may also include plague-like lesions, particularly affecting the face, ears, and extremities. CL ulcers generally exhibit minimal pain, slow progression, and raised borders (Murray, 2012; Solomon *et al.,* 2011).

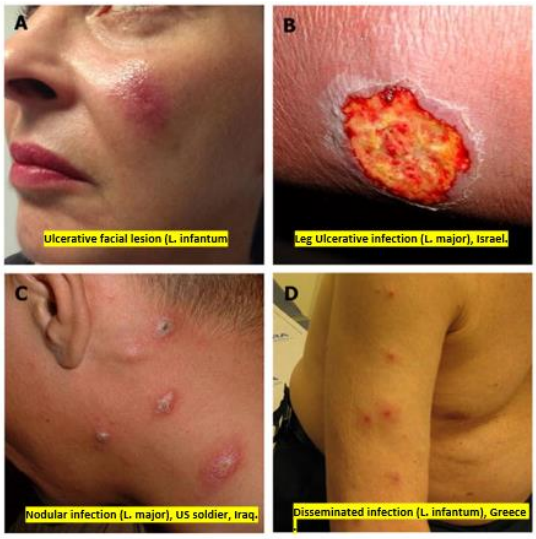

Fig. 2.1: Clinical presentation of cutaneous leishmaniasis (CL). Source: Eiras, D.P., et al., 2015

2.2.2.1. Localized cutaneous leishmaniasis:

LCL is characterized by localized warmth and swelling. Initially, an erythematous, asymptomatic papule appears at the site of the bite, though itching may occur. The papule typically ranges from 1 to 10 mm in diameter. Within 2 days, it progresses into a vesicle and later transforms into a pustule. Upon rupture, either spontaneously or due to scratching, it forms a circular ulcer with nodular or thickened borders featuring sharp, raised edges (refer to Fig. 2.2). These ulcers can persist anywhere from 2.3 to 2.5 months to as long as 15 to 20 years. The base of the ulcer displays granulation tissue that bleeds upon contact and is surrounded by a

pink margin, occasionally covered by a whitish pseudo-membrane (refer to Fig. 2.3). In certain cases, abundant discharge may lead to the formation of an adherent crust.

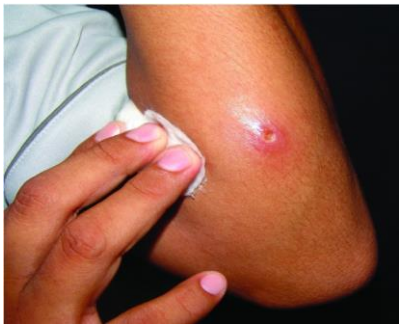

Figure 2.2: Early ulcer on the forearm with meliceric crust.

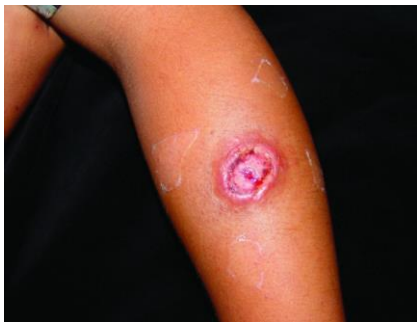

Figure 2.3: Ulcer on the upper limb with crusts and raised borders

Causative Species: *L. (L.) major, L. (L.) mexicana, L. (L.) amazonensis, L. (V.) braziliensis, L. (L.) tropica, L. (L.) aethiopica, L. (V.) panamanensis, L. (L.) infantum, L. (L.) donovani*
Source: Torres-Guerrero, E., et al., 2017

2.2.2.2. Diffuse cutaneous leishmaniasis:

This manifestation is characterized by anergy, indicating a lack of cellular immune response to parasite antigens. This allows the parasite to spread through tissue, lymph, and blood pathways, resulting in lesions across most skin areas except the scalp, and sometimes involving mucous membranes. When mucous membranes in areas like the oropharynx and nasopharynx are affected, painful nodules can develop, potentially leading to airway obstruction. This clinical manifestation presents considerable treatment challenges, does not resolve spontaneously, and can persist for up to two decades. This condition is prevalent in Central America, Amazonian Brazil, Venezuela, Ethiopia, and Kenya. It is caused by the *L. mexicana* complex (including *L. amazonensis*, *L. braziliensis*, and *L. pifanoi*) and primarily affects exposed areas such as the ears, cheeks, and extremities (Bravo & Sanchez, 2003; Reithinger *et al.,* 2007).

The initial signs often consist of firm, red nodules and reddish-brown, infiltrative plaques that can be either smooth or warty. These lesions typically emerge on the face and subsequently spread to other areas such as the extremities, buttocks, and mucous membranes. In severe instances, the entire skin surface may be affected. Additional symptoms may include lymphedema, lymphadenopathy, overall poor health and fever. (fig 2.4) (Torres-Guerrero, E., *et al.,* 2017)

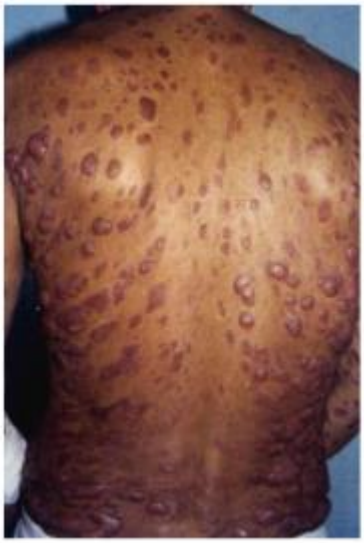

Figure 2.4: Anergic clinical form of Diffuse cutaneous leishmaniasis

Causative Species: *L. (L.) amazonensis, L. (L.) mexicana, L. (V.) pifanoi, L. (L.) aethiopica, L. (L.) major.*

Source: Torres-Guerrero, E., et al., 2017

2.2.2.3. Muco-cutaneous leishmaniasis:

Chronic treatment-resistant leishmaniasis affecting the skin and adjacent mucous membranes results from pathogen spread through lymphatic or hematogenous routes, with immunosuppression potentially triggering or exacerbating mucosal involvement. Mucosal lesions may develop during the cutaneous phase or appear years later. In South America, within endemic regions, approximately 1 to 10% of patients initially diagnosed with localized cutaneous leishmaniasis (LCL) may progress to mucocutaneous leishmaniasis within five years after apparent healing. Mucocutaneous leishmaniasis occurs in 1-3% of individuals infected with cutaneous leishmaniasis, with 90% of cases reported in Bolivia, Brazil, and Peru. The causative species, primarily from the *L. braziliensis* complex, including *L. braziliensis, L. guyanensis*, and *L. panamensis*, lead to the invasion and destruction of the nasopharyngeal mucosa (Davies *et al.,* 2000). Mucosal invasion in leishmaniasis is generally slow and may initially go unnoticed, often presenting with mild local pruritus and swelling. In Panama, a condition known as "Bejuco's ulcer," primarily affecting young individuals, is caused by *L. panamensis* (Bravo & Sanchez, 2003; Reithinger *et al.,* 2007).

Figure 2.5: Muco-cutaneous leishmaniasis ("Espundia").

Source: Prof. Dr. med. Peter Altmeyer (https://www.altmeyers.org/en/dermatology/leishmaniasis-mucocutaneous-123724#authors)

2.2.2.4. Visceral leishmaniasis, or kala-azar (black fever):

Symptoms of kala-azar typically emerge 3 to 8 months after infection, with preschool children, immunocompromised individuals, and malnourished persons being the most vulnerable. Without timely treatment, kala-azar can be fatal, highlighting the critical need for early diagnosis and intervention. Recent increases in kala-azar cases among AIDS patients and intravenous drug users suggest potential transmission through contaminated syringes. The disease often presents with lesions in the reticuloendothelial system, which may range from subclinical or oligosymptomatic cases to more severe manifestations. Common symptoms include lymphadenopathy, hepatomegaly, splenomegaly, pallor, anemia, leukopenia, thrombocytopenia, fever, night sweats, weakness, anorexia, asthenia, cutaneous pigmentation, and rapid weight loss. Affected children frequently suffer from chronic diarrhea and growth retardation (Desjeux, 2004; Guerin *et al.,* 2002).

Laboratory findings often indicate pancytopenia and hypergammaglobulinemia. If left untreated, kala-azar can progress to cachexia, multisystem failure, hemorrhage due to thrombocytopenia, and fatal secondary infections. A decline in CD4 cell count or function, particularly in patients undergoing corticosteroid therapy, chemotherapy, transplants, or those with HIV infection, may lead to disease recurrence, necessitating adjustments to therapeutic regimens (Bhat *et al.,* 2017; Collin *et al.,* 2004; Murray *et al.,* 2005).

Leishmania infection also causes a variety of cutaneous manifestations, with the species of the parasite being the primary determinant of the clinical outcome (Scorza *et al.,* 2017).

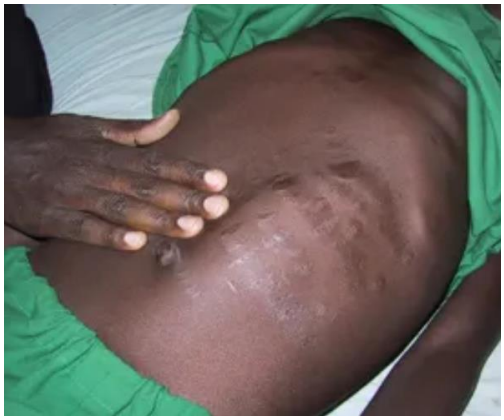

Figure 2.6: Visceral leishmaniasis
Source: https://openwho.org/courses/NTDs-visceral-leishmaniasis-east-africa?locale=es

2.2.3. Epidemiology of Leishmaniasis:

Leishmaniasis, a parasitic disease, presents a significant social and medical threat across approximately 98 countries (Alvar *et al.,* 2012; Álvarez-Hernández *et al.,* 2020; de Souza *et al.,* 2018). The disease is endemic in Asia, Africa, the Americas, and the Mediterranean region. In the Americas, leishmaniasis primarily manifests as a jungle zoonosis but can also occur in semi-desert or cold regions. Transmission is mainly through sandflies, specifically species within the Phlebotomus and Lutzomyia genera. The disease is widespread across many countries, extending from the southern United States to northern Argentina, with a sero-prevalence of cutaneous leishmaniasis (CL) at 0.017% (Hoyos *et al.,* 2016), excluding Chile, Uruguay, and El Salvador (Reithinger *et al.,* 2007). Since 2015, leishmaniasis has been recognized as endemic in the US following reports of autochthonous cases (WHO, 2017).

The distribution of leishmaniasis is influenced by various factors, including the migration and dispersal of affected individuals and animals, as well as climatic variations that facilitate disease spread (Gage *et al.,* 2008). Among the registered cases, cutaneous leishmaniasis (CL) constitutes the majority, accounting for three to four times as many cases as other forms, making it the most common variant (Hailu *et al.,* 2016). The prevalence of CL is increasing globally (Alvar *et al.,* 2012; Bailey *et al.,* 2017).

Leishmaniasis exhibits a diverse epidemiology with the highest prevalence in East Africa, Brazil, and the Indian Subcontinent. Ninety percent of visceral leishmaniasis (VL) cases are reported in Sudan, Brazil, India, Bangladesh, and Nepal (Hailu *et al.,* 2010). *Leishmania infantum* and *Leishmania donovani* are the primary species responsible for these cases. *L. infantum* is prevalent in the drier areas of Latin America and Mediterranean climate regions, while *L. donovani* is predominantly found in sub-tropical regions of Asia and Africa. VL is concentrated in Bangladesh, Brazil, Ethiopia, India, South Sudan, and Sudan, and is considered endemic in East Africa, North Africa, Central Africa, and the Horn of Africa. The disease was first reported in Niger in 1911 and later became endemic in Mauritania, Gambia, Senegal, Nigeria, and Cameroon (Menkir & Tsion, 2015). Approximately 70% of CL cases occur in

Afghanistan, Algeria, Brazil, Colombia, Costa Rica, Ethiopia, Iran, Sudan, and Syria (Guerrero *et al.,* 2017; Ready, 2014a).

East Africa ranks as the second-largest region for VL occurrences, with an estimated 30,000 cases and 4,000 related deaths, predominantly in Sudan, Ethiopia, and Kenya. VL is associated with high mortality and morbidity, exacerbated by poor nutritional status and the remote location of endemic areas (Hailu *et al.,* 2010; Al-Salem *et al.,* 2016).

In the Mediterranean region, *Leishmania infantum* is the primary cause of both visceral leishmaniasis (VL) and canine leishmaniasis (CanL) (Gramiccia *et al.,* 1989). Leishmaniasis represents a significant public health issue in the Mediterranean, with CL and VL being prevalent in 14 of 22 countries. Outbreaks occur approximately every decade. In 2008, about 100,000 new cases of CL were reported. Zoonotic cutaneous leishmaniasis, caused by *L. major* and *L. tropica*, affects countries including Afghanistan, Iran, Iraq, Morocco, Pakistan, Saudi Arabia, Syria, and Yemen. The primary endemic areas for *L. donovani*-induced anthroponotic VL are Somalia and Sudan, while zoonotic VL caused by *L. infantum* is widespread throughout most of the region (Postigo, 2010).

2.2.4. Transmission and Life cycle:

2.2.4.1. Causative Agent:

About 21 out of 30 species that infect mammals, are capable of infecting humans. This comprises three species that are part of the *L. mexicana* complex (*L. mexicana, L. amazonensis,* and *L. venezuelensis*), three species that are part of the *L. donovani* complex (*L. donovani*, *L. infantum*, and *L. chagasi*), and species like *L. tropica, L. major*, and *L. aethiopica*. Four important species (*L. (V.) braziliensis*, *L. (V.) guyanensis*, *L. (V.) panamensis*, and *L. (V.) peruviana* are also part of the subgenus Viannia. Under a microscope, these species are identical in appearance, but isoenzyme analysis, molecular techniques, or monoclonal antibodies can distinguish them (Parija S, 2004; Roberts M. T. M., 2005).

Figure 2.7. sandfly

2.2.4.2. Life Cycle:

Leishmania parasites undergo two key developmental stages: amastigotes and promastigotes. Amastigotes are spherical, non-flagellated cells, measuring 2 to 4 µm in diameter. In contrast, promastigotes are elongated, flagellated cells, resembling lances, and range from 5 to 14 µm in length and 1.5–3.5 µm in width. While various species of Leishmania do not exhibit significant morphological differences, they are categorized based on geographical, biological, and clinical characteristics. The life cycle of Leishmania involves both vertebrate hosts (e.g., humans, rats, dogs, rodents, and hyrax) and invertebrate hosts, specifically sandflies (Phlebotomus in the Old World and Lutzomyia in the New World). Promastigotes, the motile and propagative form of the parasite, develop within the lumen of the female sandfly. Upon transmission to a mammalian host via a sandfly bite, these promastigotes transform into amastigotes, which then reside within the phagolysosomes of host cells. Transmission of the parasite typically occurs when an infected sandfly bites a mammalian host, most often a human (Chhabra MB & Singla LD, 2014; Sharma & Singh, 2008; Teixeira *et al.,* 2013; Koutis CH, 2007; CDC, 2023). A summary of the life cycle is depicted in fig. 2.8.

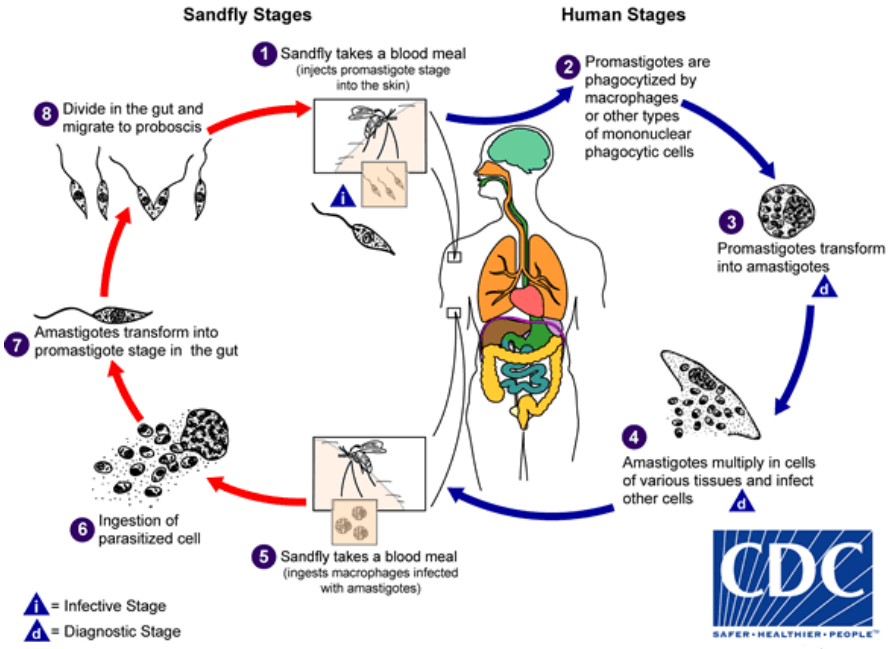

Figure 2.8: Life cycle of leishmaniasis

(source: https://www.cdc.gov/dpdx/leishmaniasis/index.html)

To summarize the figure 2.8 in which, individuals can contract the infection of leishmaniasis through the bite by an infected female sandfly, which injects a form of the protozoa known as promastigotes that can lead to infection. These promastigotes are engulfed by specific immune cells called macrophages through a process known as phagocytosis. Within these cells, the promastigotes transform into another form called amastigotes. When an infected person or animal is bitten by another sandfly, the fly becomes infected by consuming blood containing macrophages containing amastigotes. Within the midgut of the fly, the amastigotes develop into

promastigotes, which then undergo multiplication, development, and migration to the fly's mouthparts (CDC, 2023).

2.2.4.3. Transmission and Life cycle:

Leishmaniasis can spread between peoples through biting by infected female phlebotomine sand flies, which inject metacyclic promastigotes, the infective stage, into the host's skin during what is called a blood meal. Once inside the host, promastigotes are engulfed by macrophages and other mononuclear phagocytic cells, where they undergo transformation into amastigotes, the tissue stage. Amastigotes then replicate within these cells and infect other mononuclear phagocytic cells through simple division. When sand flies feed on an infected host, they ingest macrophages containing amastigotes, becoming infected themselves. Within the sand fly's midgut, amastigotes undergo transformation into promastigotes, where they multiply, develop, and migrate to the proboscis for transmission during subsequent blood meals (CDC, 2023; Ceciliop *et al.,* 2022). Summary of leishmaniasis transmission presented as follow (figure 2.9):

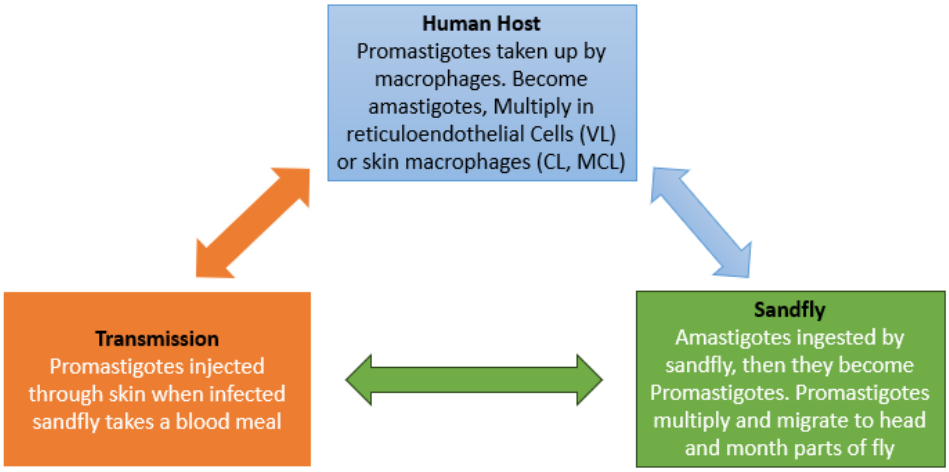

Figure.2.9: Transmission of Leishmania (prepared by researcher)

2.2.5. Diagnostic approaches of leishmaniasis:

The initial sign of infection typically appears as a small, red area at the site of the sandfly bite. As the infection progresses, the parasites induce an inflammatory response, causing the redness to develop into an open ulcer or, in some cases, spread to organs such as the spleen and liver. The severity of these inflammatory reactions varies depending on the causative *Leishmania* spp, the host's immune response, the parasite strain, and other yet unidentified factors (Reithinger & Dujardin, 2007).

Early detection and diagnosis of leishmaniasis are essential to prevent the progression to advanced, high-risk clinical stages and to reduce mortality in patients with leishmaniasis. Traditionally, diagnosis involves microscopic examination of amastigotes in tissue aspirates

from organs such as the spleen, lymph nodes, liver, and skin. Parasites can also be cultured from these sites. However, this method is uncomfortable for patients, and isolating the parasite from cultures is time-consuming, expensive, and technically challenging (Mugasa *et al.,* 2010).

There are three main diagnostic approaches for leishmaniasis, each with varying degrees of sensitivity and specificity:

2.2.5.1.1. Microscopic examination:

Microscopic examination is a considered as gold slandered tool for leishmaniasis, but it cannot specifically identify the Leishmania species. For cutaneous leishmaniasis (CL), sensitivity varies by region, ranging from approximately 50-70% for species in Africa, Asia, and Europe to 15-30% for species in the Americas. This method involves direct examination of stained lesion material, but its sensitivity can be enhanced by combining it with polymerase chain reaction (PCR). In tissue samples stained with Giemsa or hematoxylin and eosin, only the amastigote stage of the parasite is visible.

For visceral leishmaniasis (VL), spleen aspirates offer the highest sensitivity. Lymph node, bone marrow, or spleen aspirates are used to confirm Leishmania infection and identify the species through molecular methods. While microscopic examination is valuable, combining it with complementary techniques can improve diagnostic accuracy for this parasitic disease (Babiker *et al.,* 2007; Saab *et al.,* 2015; Sandoval *et al.,* 2018; Solano-Gallego *et al.,* 2009; WHO, 2015; Sousa *et al.,* 2014).

2.2.5.1.2. In Vitro Cultivation of Leishmania:

An alternative method beyond direct examination involves using a portion of the biopsied material for inoculation in a culture medium. Although rarely used in routine clinical practice, this approach allows for the isolation and in vitro cultivation of the parasite, aiding in species identification (Sundar, S.; & Rai, M, 2002)

2.2.5.1.3. Inoculation of Leishmania in Experimental Animals:

This method involves inoculating parasites obtained from patient samples into experimental animals. For cutaneous leishmaniasis (CL), the inoculation sites include the footpad, nose, or tail base of mice. For visceral leishmaniasis (VL), intravenous or intraperitoneal inoculation is performed in mice or golden hamsters (Sundar, S.; & Rai, M, 2002).

2.2.5.1.4. Xenodiagnoses:

Xenodiagnoses is a diagnostic technique that finds illnesses in patients or hosts that are mammals by using insect vectors, like sand flies, as a culture medium. This technique was more recently used to diagnose patients with visceral leishmaniasis (VL) and post-kala-azar dermal leishmaniasis (PKDL). It was initially created to be used in experimental leishmaniasis diagnosis using mice infected with *L. donovani* as a model. Both direct and indirect strategies are used in the process. It's interesting to note that Phlebotomus argentipes, a species of sand

fly, is susceptible to infection by VL and specific types of PKDL. By employing this technique to investigate the disease's transmission dynamics, researchers can stay away from utilizing human subjects (Sadlova, J., *et al.,* 2015).

Serological methods are noted for their sensitivity, specificity, and cost-effectiveness. Antibody-based diagnosis, such as the rK39 strip test, is utilized globally in affected countries, although it has the drawback of potentially yielding positive results in healthy individuals for extended periods post-cure.

The rk39 dipstick and the Direct Agglutination Test (DAT) are widely used diagnostic tools for leishmaniasis. DAT is a simple, affordable, and reliable semi-quantitative test that measures the agglutination of Leishmania parasites with anti-leishmanial antibodies (Elmahallawy *et al.,* 2014). It is suitable for both laboratory and field settings due to its ease of use and cost-effectiveness. The test provides semi-quantitative results with antibody levels ranging from 1:100 to 1:51,200, and a positive cut-off value of 1:3,200 in endemic regions (Bern *et al.,* 2000; Chappuis *et al.,* 2005; Srividya *et al.,* 2012).

These tests are instrumental in initiating treatment by enabling rapid diagnostic confirmation of Visceral Leishmaniasis (VL) at peripheral health facilities with minimal laboratory infrastructure. Recent studies in Kenya have demonstrated that the rK39 dipstick test has a high sensitivity of 97% and a specificity of 100%. However, it is important to remember that serological tests cannot differentiate between active and latent infections (Bern *et al.,* 2000; Chappuis *et al.,* 2005).

Molecular methods offer even greater sensitivity and represent a powerful tool for early parasite detection. Although many molecular diagnostic techniques have been successfully employed for leishmaniasis diagnosis, their primary use remains within research laboratories due to the need for skilled personnel. Implementing these methods in clinical settings and health facilities, particularly in resource-limited and developing regions, is challenging due to the scarcity of adequately trained personnel.

In a study comparing microscopy and culture methods to distinguish Leishmania species based on internal transcribed spacers ITS-PCR, it was discovered that ITS-PCR is not only valid for species identification but also has a high sensitivity and specificity (98.8% and 100%, respectively) when compared to parasitological methods of diagnosing CL (79.6% and 86.2% sensitivity respectively) (Shahbazi, F., *et al.,* 2008).

2.2.5.1. Others Diagnostic Methods:

Western blotting method

The Western blotting method, though infrequently employed, involves transferring proteins onto a nitrocellulose or nylon membrane following their separation by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). This technique is utilized in diagnosing both cutaneous and visceral forms of leishmaniasis, specifically for detecting the Leishmania genus (Reithinger & Dujardin, 2007).

NFGT or the Aldehyde test

Napier's Formal Gel Test involves mixing a small quantity of serum or plasma with a drop of 37% formaldehyde solution. Results are available within 20-30 minutes, with a positive outcome indicated by rapid coagulation or precipitation. This test is used for detecting cutaneous leishmaniasis, specifically identifying the Leishmania genus (Chappuis *et al.,* 2005; Solano-Gallego *et al.,* 2009).

Montenegro test

The Leishmania skin test, also known as the Montenegro test, evaluates delayed-type hypersensitivity by injecting 5 x 10^7 phenol-killed promastigotes into the forearm. The test result is determined by measuring the induration that forms after 48 to 72 hours (Bern *et al.,* 2006).

The following table summarizes different methods used for leishmania diagnosis (adapted from Reimão, J *et al.,* 2020).

Table 2.2: Description of the primary techniques for CL and VL diagnosis.

Method	**Visceral Leishmaniasis (VL)**	**Cutaneous Leishmaniasis (CL)**
Parasitological Methods		
Microscopic examination (biopsy, punch, scraping, smear, imprinting)	No	Yes
Bone marrow, lymph nodes, spleen aspirates, or liver biopsy followed by microscopic examination	Yes	No
In vitro cultivation	Yes	Yes
Inoculation in animals (mice or hamsters)	Yes	Yes
Xenodiagnosis	Yes	No
Protein-based Methods		
MLEE	Yes	Yes
Monoclonal antibodies	Yes	Yes
MALDI-TOF MS	Yes	Yes
KAtex	Yes	No
DNA-based Methods		
PCR-RFLP	Yes	Yes
DNA sequencing	Yes	Yes
Real-time PCR	Yes	Yes
PCR-HRM	Yes	Yes
MLST	Yes	Yes
LAMP	Yes	Yes
Immunological-based Methods		
Leishmania skin test	No	Yes (negative for DCL)
ELISA (rK39)	Yes	No
ELISA (other recombinant antigens)	Yes	Yes
IFAT	Yes	Yes
DAT	Yes	No
ICT (rK39)	Yes	No
Dipstick test [L. (L.) donovani promastigote antigens]	Yes	No
Western blot	Yes	Yes

2.2.6. Treatment of Leishmaniasis:

The treatment approach for leishmaniasis is determined by factors such as the causative species, geographic location, disease severity, and type (CL, VL, ML, PKDL). Successful treatment relies on the patient's immune system. However, challenges like drug resistance and significant side effects have emerged due to misuse, leading to the exploration of alternative treatments, including the use of plants and herbs (Oliveira RMD *et al.,* 2018). This form of treatment, known as phytotherapy, is particularly important in developing countries with limited healthcare resources, as it can enhance the immune system (Cragg *et al.,* 2009; Jantan *et al.,* 2015). For instance, combining miltefosine with curcumin nanoparticles has been shown to improve lymphocyte proliferation and macrophage phagocytic activity (Tiwari *et al.,* 2017).

2.2.6.1. Treatment of Cutaneous leishmaniasis (CL):

Topical medications, cryotherapy, thermotherapy, and intralesional injections are commonly used to treat cutaneous leishmaniasis (CL). For the best outcomes, combining cryotherapy with intralesional antimonials is recommended. Treatment strategies vary depending on the Leishmania species and geographic location. For treating *L. recidivans*, options include cryotherapy, paromomycin-based ointments, and intralesional antimonials. Systemic treatments include oral fluconazole, ketoconazole, miltefosine, liposomal amphotericin B (LAMB), pentavalent antimonials (with or without pentoxifylline), and pentamidine isethionate (WHO, 2015b).

2.2.6.2. Treatment of Mucocutaneous leishmaniasis:

For this form of leishmaniasis, systemic treatments include pentamidine isethionate, pentavalent antimonials combined with pentoxifylline, and liposomal amphotericin B (LAMB) (WHO, 2015b).

2.2.6.3. Treatment of post-kala-azar dermal leishmaniasis:

The treatment approach for post-kala-azar dermal leishmaniasis (PKDL) varies by region. In East Africa, most cases are self-healing and do not require intervention, whereas in the Indian subcontinent, treatment is primarily administered for cosmetic purposes. The WHO recommends miltefosine, amphotericin B deoxycholate, and liposomal amphotericin B (LAMB) for patients in the Indian subcontinent. For East Africa, the recommended treatments include pentavalent antimonials, LAMB, miltefosine, and combination therapy (pentavalent antimonials with paromomycin), based on evidence grading (WHO, 2015b).

2.2.6.4. Treatment of Visceral leishmaniasis:

Pentavalent antimonials, once the standard treatment for visceral leishmaniasis (VL), have become less effective in the Indian subcontinent due to emerging resistance. In East Africa, these antimonials are still used alongside LAMB and paromomycin, with LAMB preferred for severe cases and vulnerable patients. In Asia, sodium stibogluconate remains the primary treatment for *Leishmania infantum* and *Leishmania donovani*. The WHO's initial recommendation of LAMB

for the Indian subcontinent has evolved to include various drug combinations to address resistance issues (Balasegaram *et al.,* 2012; Buraz S *et al.,* 2018).

Treatment of CL in Palestine is available exclusively and free of charge by the PMoH. This include intramuscular pentavalent antimonial sodium stibogluconate (Pentostam) (10–20 mg/kg body weight) daily for 10–20 days (Amro *et al.,* 2022).

2.2.7. Risk Factors:

Environmental factors, socioeconomic conditions, and demographic characteristics have a substantial impact on human health, particularly concerning vector-borne diseases such as leishmaniasis (Oryan & Akbari, 2016). Borges, M. S., *et al.,* (2022). The factors associated with the expansion of leishmaniasis in urban areas are interrelated, including socioenvironmental and economic complexity, the type of leishmaniasis, the reservoirs, vectors, deforestation, disorderly occupation of space, poor sanitary conditions, and human migration trends. Key risk factors for leishmaniais include:

Socio-demographic/economic factors:

The likelihood ratio or chance of contracting leishmaniasis is going in parallel manner with poverty situation of people. Poor and inadequate residential and hygiene conditions, such as lacking or insufficient or poor waste disposal or exposed (i.e., opened) sewage systems can lead to more breeding and resting places (suitable environment) for existence and reproduction of sandflies, as well as greater human exposure. Furthermore, crowded houses with more family members give more opportunities to sandflies to bite people and feed on their blood due to their behavior such as sleeping outdoor in open air environment or laying on the ground (earth) also leading to increase the likelihood of people to get leishmaniasis infection.

Studies indicate that VL is prevalent among poorer populations, with 83% of cases in India affecting the poorest 40% (Boelaert *et al.,* 2009; Pascual Martínez *et al.,* 2012). Similarly, VL is more common among the impoverished in Kenya and other regions (Argaw *et al.,* 2013; Kolaczinski *et al.,* 2008; Okwor & Uzonna, 2016; Uranw *et al.,* 2013). Poverty also remains a key factor in leishmaniasis spread, as evidenced by Hakkour *et al*. (2020), who highlighted its impact alongside proximity to endemic areas in Morocco. Amane M. *et al.* (2022) in a case-control study in Morocco found that socioeconomic factors such as poverty and rural habitation contribute significantly to the risk of cutaneous leishmaniasis (CL). Avar *et al.,* (2006) found that increasing in CL prevalence is linked to poverty. Mandal PK, *et al* (2019), El Alem MMM, *et al.,* (2018) and Oryan A,*et al* (2016) found that poverty could be the main determinant of the transmission of leishmaniasis, especially its visceral form, as well as the cutaneous form.

Indoor and Surrounding Factors:

Indoor and surrounding conditions significantly affect leishmaniasis risk. Living near ant hills, acacia trees, and specific vegetation increases human contact with sandflies. Poor housing conditions, such as those found in dilapidated and thatched structures, are associated with higher VL prevalence (Bern *et al.,* 2010). Factors like damp floors and cracks in homes, as well as pet

ownership, are linked to increased risk (Bern *et al.,* 2000). Ocampo *et al.* (2012) identified that areas with higher disease transmission rates often have more forested regions and shade-grown coffee, which attract sandflies. Yared *et al.* (2014) found that living in houses with shattered walls and spending more time in agricultural fields are associated with higher VL risk. Improvements in housing and the use of bed nets can mitigate these risks. Poor housing and inadequate waste management create favorable conditions for sandfly breeding, increasing disease risk. Overcrowded and unsanitary living conditions, particularly in impoverished areas, exacerbate the problem. In Turkana County, for instance, rapid urban growth has worsened living conditions, contributing to higher rates of visceral leishmaniasis (VL) (Desjeux, 2004; Hasker *et al.,* 2012)

Malnutrition and Co-morbidity:

Shortage in food both quantity and quality and nutritional habits and behaviors can play a crucial role in the management and outcome of several diseases including Leishmaniasis. Malnutrition can exacerbate the severity of the infection and affect the body's ability to fight off the disease. This malnutrition or inadequate nutrition is characterized by insufficient intake of protein-energy, iron, vitamin A, and Zinc intake elevates the likelihood that an infection will develop into advanced severity stage of illness. Factors such as malnutrition, displacement, poor housing conditions, weakened immunity, and low socioeconomic status are linked to the disease (WHO, 2020). Malnutrition and co-morbid conditions exacerbate leishmaniasis severity. Protein-energy malnutrition and deficiencies in iron and vitamin A are linked to severe VL (Daher *et al.,* 2017; Ready, 2014b). Malnutrition impairs the immune system, increasing disease severity (Cerf *et al.,* 1987). Intestinal parasites, which contribute to poor nutritional status, are also associated with severe VL (Jardim-Botelho *et al.,* 2008; Mengesha *et al.,* 2014).

Human Behavioral Factors:

Human behaviors, such as outdoor sleeping and proximity to animals, influence leishmaniasis risk. In Uganda, low income, proximity to animal pens, and mosquito net ownership were identified as factors affecting VL risk (Kolaczinski *et al.,* 2008). Seasonal and migratory patterns contribute to disease spread (Sharma & Singh, 2008). Studies from Shaanxi and Shanxi, China, highlight the impact of environmental, meteorological, and socioeconomic factors on VL prevalence (Zhao *et al.,* 2021). War and socio-conflict also exacerbate leishmaniasis (Oryan & Akbari, 2016c). Behavioral patterns, including outdoor sleeping and migration, are significant risk factors. A case-control study examined 62 cases treated at healthcare facilities and 248 randomly selected controls from the same villages. Identified risk factors included residing in thatched houses, sleeping on the ground floor, owning animals, relocating to specific areas, and being within 50 meters of known VL cases. Education was found to offer protection against VL, and socioeconomic status demonstrated a clear dose-response relationship, with the odds of VL decreasing as socioeconomic status improved. The study highlights the need to enhance surveillance, awareness programs, and conduct further comprehensive research on risk factors, vectors, and control strategies for VL (Mandal *et al.,* 2020). In Ethiopia's highlands, outdoor sleeping and activities elevate the risk of infection (Custodio *et al.,* 2012), with men being particularly vulnerable due to their involvement in agricultural work (Malaria Consortium, 2010).

Livestock, Individual Movement, and Political Factors:

Livestock movement and individual migration patterns impact leishmaniasis spread. Seasonal migrations and herding activities, as observed in Ethiopia, influence VL risk (Gebremichael Tedla *et al.,* 2018). In Europe, the movement of people and animals from endemic regions has contributed to VL resurgence (Ready, 2010). In Iraq, environmental, human behavioral, and vector dynamics factors affect VL epidemiology, emphasizing the need for advanced diagnostic techniques and targeted control measures (Jarallah *et al.,* 2022). Amro A., *et al.,* (2009) found that VL increased among people who had domestic dogs and/or other animals (OR 2.4; 95% CI 1.19-4.68; P=0.017). Araujo AR, *et al.,* (2016) and Amane M. *et al.* (2022) identified that the presence of livestock and the placement of companion animals in close proximity to habitants increase the risk of ACL. This is consistent with previous investigation that confirms an association between cutaneous leishmaniasis and keeping animals at home and in peri-domestic area.

Epidemics and outbreaks of leishmaniasis often occur when a large number of non-immune individuals relocate or travel to regions with a high rate of infection and the transmission opportunities. El Miri H, *et al.,* (2016) noticed that the movement of people from rural to urban area, where housing conditions are unfavorable, contributes to the emergence of the disease. The incidence of leishmaniasis has risen in the recent years. The numbers are anticipated to keep rising due to increasing human mobility, including travel and forced migration, growing reservoir host populations as well as expansion and dispersal of vector species caused by climate and habitat changes, urbanization and globalization (Riebenbauer, K., *et al.,* 2024). The increase in CL is associated with poverty and migration caused by war (Ozaras *et al.,* 2016; Raad *et al.,* 2018).

In Palestine there are several factors contributing to the increasing CL incidence. These include human immigration to endemic areas, urbanization and agricultural activities, land use, and climatic and environmental conditions. However, migration of CL cases in Palestine is not easy to predict and was not quantified (Amro, A., *et al.,* 2022).

Environmental factors and climate change:

Environmental and climatic changes significantly influence the prevalence of leishmaniasis, with the disease often occurring in rural areas but also emerging at the edges of urban centers. Environmental shifts and climate change can facilitate the spread of sandfly vectors, potentially broadening the disease's global reach. Urban expansion, deforestation, and human intrusion into forested areas further contribute to the rise in leishmaniasis cases. Climatic factors like temperature fluctuations and changes in precipitation patterns can alter sandfly populations, increasing the disease's prevalence. Extreme weather events, such as droughts, famines, and floods, can force human migration to regions with higher parasite transmission rates. Specific climatic conditions, such as temperature, humidity, and rainfall, are crucial in determining the prevalence of leishmaniasis (Short *et al.,* 2017). For instance, in Bam County, leishmaniasis is found in both urban and rural areas with particular climatic conditions (Ghatee *et al.,* 2023). A 1°C increase in air temperature was linked to more VL cases in Montenegro (Medenica *et al.,* 2023). Climate change, including global warming and land degradation, affects vector distribution and leishmaniasis transmission (Asfaram *et al.,* 2017). In Colombia, climate

variations significantly influenced leishmaniasis rates (Cardenas *et al.,* 2006), and warmer climates and specific rainfall patterns were associated with higher VL incidence in India and Bangladesh (Abdullah & Al-Moslih, 2005; Hasker *et al.,* 2012).

The presence of toilets, water pipes and, consequently, a sewage disposal system reduces the incidence of leishmaniasis (Araujo AR, *et al.,* 2016). Indeed, housing conditions and domestic hygiene are major determinants in the spread of VL (Oryan A, Akbari M., 2016) and cutaneous leishmaniasis (Bamorovat M, *et al.,* 2018), as they may increase the breeding and rest biotopes of sand flies, as well as their access to humans. Improved housing conditions and personal protection efforts by the poor have the potential to reduce the incidence of visceral leishmaniasis (Mandal PK, *et al.,* 2019).

2.2.8. Control and Prevention:

Effective and successful management of VL can be realized by implementing strategies to reduce human-vector interaction, as suggested by Sharma & Singh (2008). These strategies include:

- Utilizing bed nets treated with insecticides such as permethrin (used by the Palestinian ministry of health), lambda-cyhalothrin, and deltamethrin to create a protective barrier (Bongiorno *et al.,* 2005).
- Indoor residual spraying (IRS) involves the community in spraying the inside walls of homes with suitable insecticides in both domestic and surrounding areas.

Personal protection measures:

- Indoors (inside house): Installing fine-mesh screens on windows and doors, using curtains treated with insecticides, mosquito coils, and burning leaves known to repel sandflies.
- Outdoors (outside house): Applying skin or clothing repellents like diethyltoluamide and wearing protective clothing such as long-sleeved shirts, trousers, boots, and hats, especially in areas where VL is prevalent (Asfaram *et al.,* 2017).

Modifying the physical environment to disturb the habitats conductive to the breeding and proliferation of vectors and parasites. This includes sealing gaps in the structure of homes and managing vegetation and debris around living spaces to minimize sandfly habitats.

Destroying potential breeding sites near homes, such as animal burrows and unused termite mounds (Cardenas *et al.,* 2006), and promoting health education among local health workers and the community.

Regular vaccination and examination of wildlife and domestic animals, which serve as reservoir hosts for the disease to prevent zoonotic transmission of leishmaniasis (Cardenas *et al.,* 2006).

In Palestine, the responsibility for epidemiological surveillance and monitoring of leishmaniasis cases falls under the Palestinian Ministry of Health, specifically the Department of Preventive

Medicine and the Department of Environmental Health. The Department of Preventive Medicine, through its preventive medicine sections distributed across all governorates, receives potential cases, conducts examinations, and collects samples for laboratory testing to confirm the infection. Once the infection is confirmed, medical treatment is promptly initiated.

On the other hand, the responsibility of the Department of Environmental Health, through its environmental health sections spread across all governorates, is to follow up on cases referred by the Department of Preventive Medicine after confirmation. Environmental health officers visit these cases at their residences to assess the home environment and surrounding areas, searching for potential sources, reservoirs, and breeding grounds for the vector, the sandfly. They then engage in environmental control efforts with the family, such as cleaning any unclean areas, followed by chemical control using insecticides.

Annually, the Department of Environmental Health, through its sections in all governorates, conducts three insecticide spraying campaigns in collaboration with municipalities and local councils. These campaigns target homes with confirmed cases and their surroundings, as well as active hotspots. Additionally, the department implements awareness and education campaigns about the disease, its causes, and transmission methods in collaboration with municipalities, schools, associations, and clubs (Ministry of Health (MOH), Preventive medicine and Environmental Health Departments, 2023 (personal communication)).

2.2.9. Leishmaniasis in Palestine:

The Ministry of Health's annual report states that the CL occurrence rate (the average annual incidence rate (AAIR)) was 1.16 cases per 10^5 population in the whole Palestine and 2.02 cases /10^5 population in West Bank, while the incidence rate of VL (the average annual incidence rate (AAIR)) was 0.02 cases per 10^5 in Palestine and 0.04 cases per 10^5 in West Bank (Ministry of Health (MOH), 2022). There was a fluctuation in the incidence of both CL and VL in Palestine during last 7 years, but it seems that the incidence is declined overtime (Table 2.3) (Ministry of Health (MOH), Preventive medicine and Environmental Health Departments, 2023 (personal communication)).

Table 2.3: Fluctuation in the incidence rate /100,000 of CL and VL over the period between 2015-2022 (Ministry of Health, 2023) *

Year	2015-2016		2016-2017		2017-2018		2018-2019		2019-2020		2020-2021		2021-2022	
	WB	**PAL**	**WB**	**PAL**	**WB**	**PAL**	**WB**	**PAL**	**WB**	**PAL**	**WB**	**PAL**	**WB**	**PAL**
CL	13.5	8.3	8.3	4.9	10.6	6.1	7.5	4.4	6.2	3.6	2.3	1.3	1.16	2.02
VL	0.14	0.09	0.11	0.07	0.12	0.07	0.27	0.15	0.19	0.11	0.07	0.04	0.02	0.04

**No data available for period of 2010-2014*
PAL: Palestine, WB: West Bank, CL: Cutaneous Leishmaniasis, VL: visceral Leishmaniasis

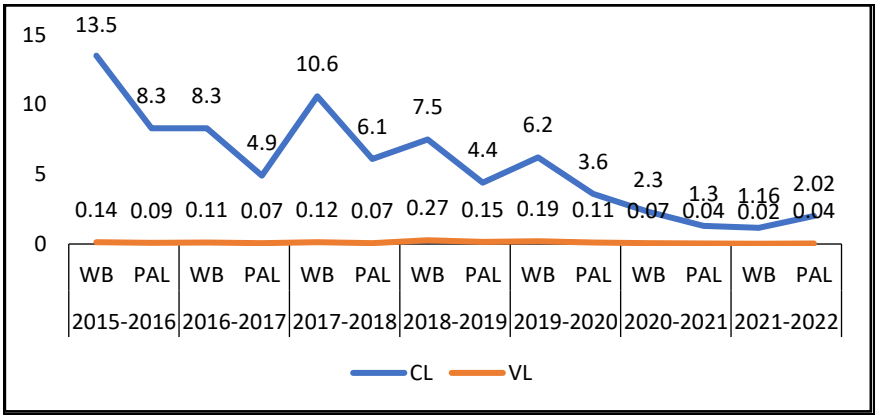

Figure 2.10: Annual rate of human CL and VL in Palestine between 2015–2022

In the West Bank, CL accounted of approximately 1.9% of all parasitic infections in Palestine, primarily caused by *L. tropica* and *L. major*. Between 2008 and 2017, there were 2.672 reported cases of CL and 40 cases of VL across various districts. The highest incidences were recorded in the district of Jericho, Tubas, Jenin, and Hebron as detailed in the accompanying table

Table 2.4: Total number of CL and VL cases over the period between 2008-2017*

District	CL	VL
Bethlehem	191	1
Hebron	228	19
Jenin	462	2
Jericho	603	0
Jerusalem	43	0
Nablus	218	2
Qalqelia	136	0
Salfit	107	2
Ramallah	87	11
Tubas	503	0
Tulkarem	94	3
Total	**2672**	**40**

** MOH, Environmental Health and preventive medicine Department, 2023(personal communication))*

The data in Table (2.5) below shows a general decline in the number of new Cutaneous Leishmaniasis (CL) cases across various districts in Palestine from 2015 to 2022, with total cases dropping from 387 in 2015 to 85 in 2022. Notably, districts like Jericho and Tubas experienced significant spikes early on but saw substantial decreases in subsequent years. While Hebron displayed relatively stable numbers with minor fluctuations, other districts, including Bethlehem, Jenin, and Nablus, reported marked reductions over time. Despite the overall decline, some districts showed a slight resurgence in cases in the later years, indicating the need for sustained public health efforts to maintain control over the disease (MoH annual reports, 2016, 2017, 2018, 2019, 2020, 2021, 2022, 2023).

Table 2.5: Number of CL Lisheminiasis new cases according to year of infection *

District	2015	2016	2917	2018	2019	2020	2021	2022
Bethlehem	11	6	6	12	1	0	9	3
Hebron	32	30	33	12	13	16	19	23
Jenin	36	16	43	16	5	2	0	1
Jericho	71	92	51	27	11	4	12	20
Jerusalem	6	6	2	1	2	0	5	5
Nablus	33	13	22	21	18	3	3	9
Qalqelia	20	9	15	24	4	2	1	2
Salfit	20	1	14	4	6	2	2	0
Ramallah	12	9	10	2	7	2	0	3
Tubas	110	27	67	30	13	3	12	16
Tulkarem	36	12	10	8	2	0	3	3
Total	**387**	**221**	**273**	**175**	**101**	**54**	**87**	**85**

**MOH annual reports*

Amro *et al.*, (2009) found that the three Leishmania species; *L. tropica* and *L. major* are responsible for CL, while *L. infantum* is associated with VL, and leishmaniasis in dogs. are existed in the West Bank. It was found that VL is existing in the western villages of the West Bank near the VL endemic Zones of Israel (no data from Gaza Strip). However, there is a significant gap in data regarding CL caused by *L. tropica* in Palestine.

Leishmaniasis was prevalent in all Palestinian regions except Gaza in 2003, with over 10 cases per 100,000 in the West Bank (Ministry of Health-PHIC, 2004). In Jerusalem and surrounding areas, CL incidence rose from 0.13 (1999-2003) to 9.7 (2004-2005) per 100,000 (Singer et al., 2008). Tiberias district reported the highest rate of 62.5 per 100,000 (Vinitsky *et al.*, 2010). Jenin district saw numerous CL cases caused by *L. tropica*, averaging 23.0 per 100,000 annually between 2002 and 2000 (Azmi *et al.*, 2017).

The Palestinian ministry of health has documented three main significant outbreaks of leishmaniasis. Reports indicated that in 1996, there were 150 recorded infections; by 2004, the figure had surged to over 250; and in 2015 the cases rose to approximately 380 (Fig. 2.10).

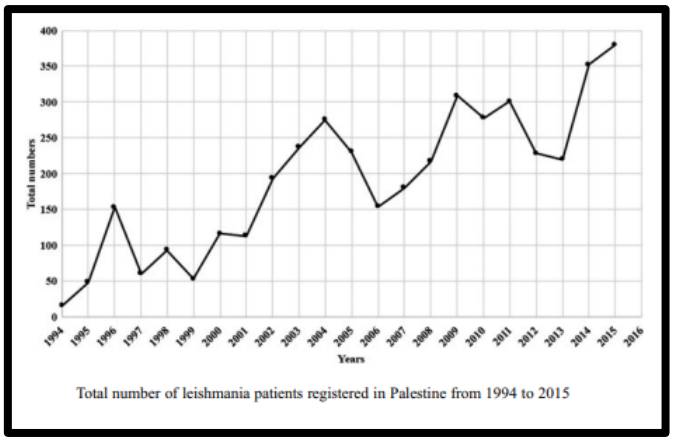

Figure 2.11: Total number of leishmaniasis patients registered in Palestine from 1994 to 2015 (Amro, 2017)

It was reported that the total VL cases was 340 in Palestinian population in West Bank (no data from Gaza) with annual incidence rate of 0.73 case/100.000 individuals during the period 1990-2017.

2.10 Conclusion remarks

Leishmaniasis remains a significant public health concern in Palestine, characterized by the presence of both cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL). The epidemiological landscape of these diseases varies across the West Bank and Gaza Strip, influenced by environmental, climatic, and socio-political factors. Over the past three decades, multiple studies have been conducted to understand the distribution, incidence, and future projections of leishmaniasis in the region, providing valuable insights for public health interventions.

Cutaneous leishmaniasis (CL) has been particularly prevalent in several regions of the West Bank, with a notable concentration of cases in Jenin, Jericho, and Tubas. A comprehensive study conducted by Amro *et al.,* (2022) examined the eco-epidemiological parameters and spatiotemporal projections of CL in Palestine over a 30-year period, from 1990 to 2020. The study reported a total of 5,855 cases during this period, with an average annual incidence rate (AAIR) of 18.5 cases per 100,000 population. The highest number of cases was recorded in Jenin (29%), followed by Jericho (25%) and Tubas (12%), with no cases reported in the Gaza Strip. The study also identified *Leishmania tropica* as the predominant causative agent, with *Phlebotomus sergenti* as the main vector. Future projections suggest an increasing incidence of CL in the northwestern parts of the West Bank and the potential emergence of new endemic foci in the Gaza Strip, driven by changes in climate.

Another significant study by Azmi *et al.,* (2012) focused on the CL situation in Jenin District between 2002 and 2009, where 466 cases were reported. This study confirmed the predominance of *Leishmania tropica* and highlighted the role of *Phlebotomus sergenti* as the vector. The findings also suggested that CL in Jenin is a zoonotic infection, although an animal reservoir has yet to be identified. Similarly, research conducted by Al-Jawabreh *et al.,* (2004) in Jericho revealed a high prevalence of both *Leishmania tropica* and *Leishmania major* among the population, with the study being the first to identify *L. tropica* in the Jericho area on a large scale.

Visceral leishmaniasis (VL), while less widespread than CL, remains a persistent health issue, particularly among children in the West Bank. A study by Amro *et al.,* (2009) documented 76 cases of VL in the Hebron district between 1993 and 2007, all of which affected children under nine years old. The causative agent was identified as *Leishmania infantum*, with *Phlebotomus syriacus* and *Phlebotomus tobbi* recognized as the main vectors. The study also highlighted a high seropositivity rate among children in households with previous VL cases and among those living in close proximity to domestic dogs. Further research by Ahmad A. (2020) expanded the understanding of VL in Palestine by analyzing its spatiotemporal patterns over a 27-year period. This study found that VL predominantly affected the western parts of the West Bank, with future projections indicating a possible disappearance of VL endemic foci in most regions, except for the very northwest of the West Bank.

In addition to these specific studies on CL and VL, a broader analysis by Hamarsheh and Amro A. (2020) provided an overview of parasitic infections in Palestine from 2008 to 2017, including leishmaniasis. This study reported a total of 137,106 cases of parasitic infections, with a higher burden in the Gaza Strip (67%) compared to the West Bank (33%). The authors emphasized the need for targeted control measures and public health education to reduce the incidence and burden of parasitic infections, including leishmaniasis, in Palestine.

These studies collectively highlight the ongoing challenges posed by leishmaniasis in Palestine, with significant regional variability in disease distribution and future risks. The findings underscore the importance of continuous surveillance, vector control efforts, and public awareness campaigns to mitigate the impact of leishmaniasis on the Palestinian population.

CHAPTER THREE: METHEDOLOGY

In this chapter the researcher will present methodologies that have been followed in order to complete this study. Starting from preparing till gathering needed data and analyzing them leading to findings and recommendations

3.1 Study area

This study was conducted among all public health departments / the preventive medicine division in southern parts of West Bank (Hebron and Bethlehem Governorate).

3.1.1. Hebron Governorate:

Covering an area of 1,060 square kilometers (410 sq. mi) as shown in figure 3.1, the Hebron Governorate is the most expansive and populous of the 16 governorates within the state of Palestine, with an estimated population of 884830 inhabitants. It encompasses 7 cities and 18 towns (Palestinian Central Bureau of Statistics (PCBS), 2021).

3.1.2. Bethlehem Governorate:

The Bethlehem Governorate, which is one of Palestine's 16 administrative divisions, encompasses a segment of the West Bank located to the south of Jerusalem. It spans approximately 660 km², as indicated in Fig. (3.2). This governorate is composed of 10 municipalities, 3 refugee camps, and 58 localities. The estimated population was 259615 (PCBS, 2021).

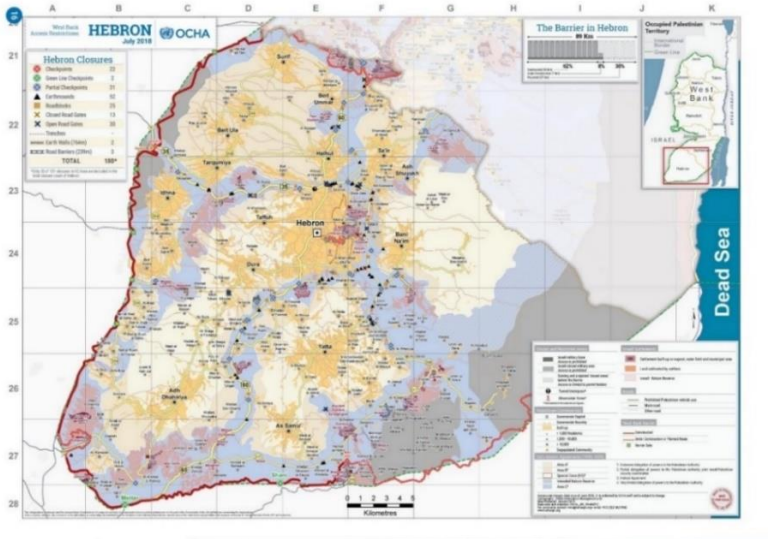

Figure 3.1: Map of Hebron District, West Bank
Source: https://www.ochaopt.org/atlas2019/wbclosure.html

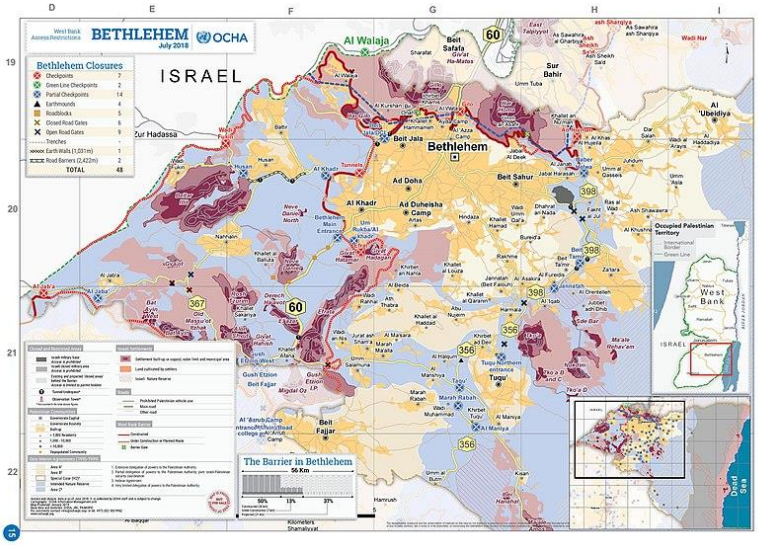

Figure 3.2: Map of Bethlehem District, West Bank
Source: https://www.ochaopt.org/atlas2019/wbclosure.html

3.2. Study design

To address the research question, a case-control study design (Fig. 3.3) was employed. Because case-control studies are effective for rare diseases, cost-effective, can examine multiple risk factors, helpful in generating hypotheses, time-efficient, and allow for confounding variable control, they are particularly well-suited to investigate the impact of social and environmental determinants on leishmaniasis occurrence. By matching cases and controls based on confounding characteristics (such as age or gender), case-control studies can be used to isolate the impact of particular social and environmental factors on the risk of contracting leishmaniasis. These characteristics make it an effective tool for understanding the complex picture stands behind leishmaniasis occurrence in a particular population.

While case-control studies are especially well-suited for studying rare diseases such as leishmaniasis, other study designs, such as cohort studies, have significant disadvantages such as being costly and time-consuming because long-term follow-up is required to detect disease development, particularly in the case of uncommon conditions like leishmaniasis.

Observing sufficient cases requires a large sample size, which might lead to additional expenses and practical difficulties. Furthermore, bias may be introduced by loss to follow-up if study dropouts differ from study participants. Confounding variables are a problem for cohort studies as well because over time, unidentified or unknown factors may affect the results (https://www.ajodo.org/article/S0889-5406(14)00542-3/fulltext).

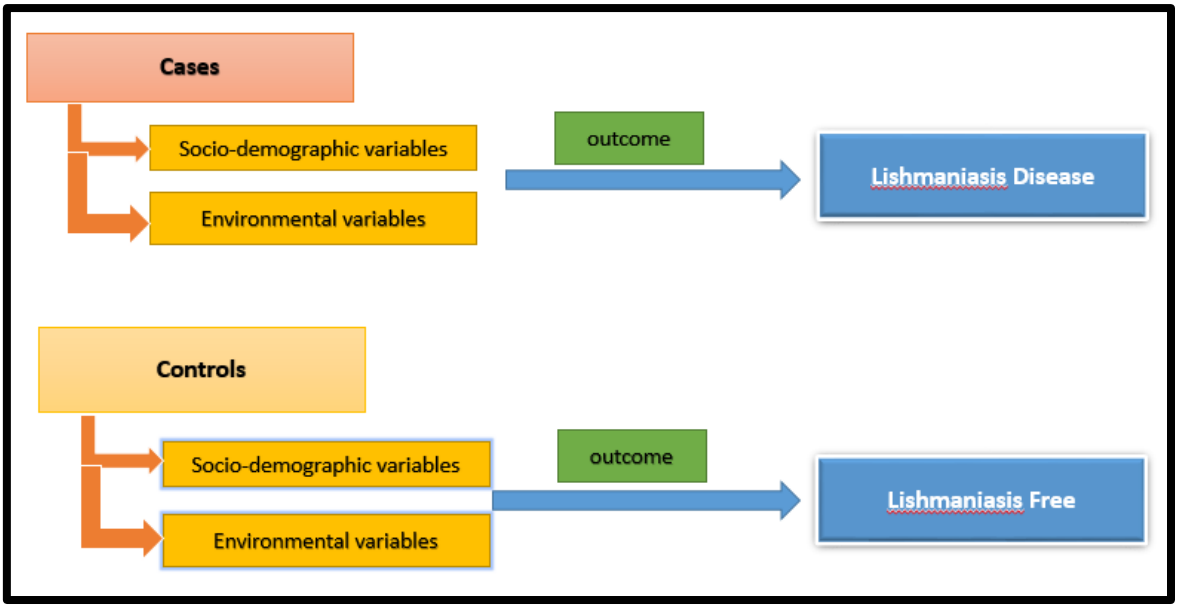

Figure 3.3: Study Design (Prepared by Researcher)

3.3 Inclusion and Exclusion Criteria

All patients who diagnosed and registered at the preventive medicine divisions/ ministry of health in both governorates were included in this study. Individuals who could not be in their village, had passed away, or were unreachable by telephone due to different reasons were not recruited in this study. The study did not put any age limits.

Disease free persons from the same patients' families living and staying in the same house and neighborhoods during the period of infection and at least for one year later.

3.4 Study population

Both populations of both Hebron and Bethlehem Governorates formed the population of this study included all registered patients for cases. The total registered cases in the preventive medicine department for both Hebron and Bethlehem districts was 402 cases (accumulated cases since 2010 (MOH, data register, 2024)).

3.5 Sample size

The sample for cases had been selected from the study population (402 registered cases) randomly (convenience sample) based on a model proposed by Yamane, (1967), which shows the following relationship.

$$n = N/ (1+Ne^2)$$

Where,

N = population size which is 402
n = sample size
e = confidence interval (0.05)

$$n = N/ (1+Ne^2)$$
$$n = 402/ [1+402(0.05)^2]$$
$$n = 402/ (1+402(0.0025))$$
$$n = 402/ (1+402(0.0025)$$
$$n = 402/2.005$$
$$n = 200.49$$

n = 200 respondents.

So, the sample size for cases required was 200 cases from both governorates. For controls, the study adopted the individual matching way (2 controls per one case). Matching increases the efficiency of the estimates if the matching variables are associated with both the disease and the exposure. Mixed matching ratios (meaning that, for example, some pairs are matched in a ratio of 1:2, between exposed and unexposed people) will not cause bias if matching variables or matched sets are adjusted for in the analysis (Iwagami, M., & Shinozaki, T. (2022); Hennessy *et al.*,1999).

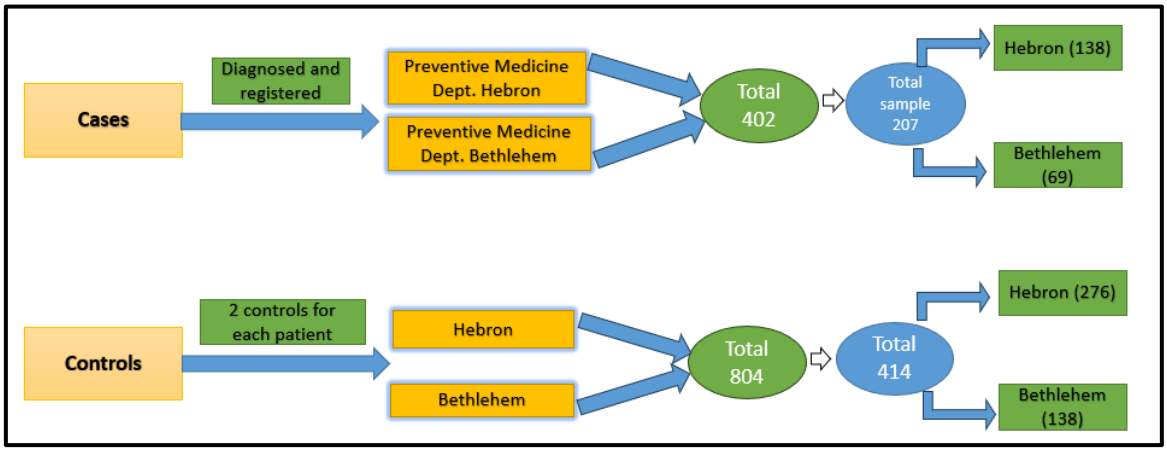

Figure 3.4: The proposed sample selection process (prepared by researcher

Therefore, the required number of participants (cases) for this study was 200 respondents. We intended to include all registered cases in the study, but due to different reasons mainly related to not reachable and availability we reached only to 207 cases (138 from Hebron and 69 from Bethlehem). For these 207 cases we included 414 as controls, So the final sample size was 621 participants (414 (66.7%) controls vs. 207 (33.3%) cases).

3.6 Data Collection

3.6.1. Questionnaire:

All information and data needed to answer the research questions and achieve the research objectives were gathered by a semi-structured questionnaire (Appendix 1). The questionnaire was adopted from previous studies (Wijerathna, T., *et al.,* (2020; Oliveira, C. D., *et al.,* (2006); Cerbino Neto J *et al.,* 2009). after applying some modifications to be suitable for the local context. The original copy of the questionnaire included questions in both English and Arabic. The questionnaire consisted of different sections as follows:

Section one: includes socio-demographic and personal information (i.e., district, age, sex, marital status, education, main occupation, residence place, monthly income, and travel to endemic area)

Section two: includes environmental factors and indoor characteristics.

Section three: includes knowledge about leishmaniasis.

Section four: includes behavioral characteristics and prevention measures.

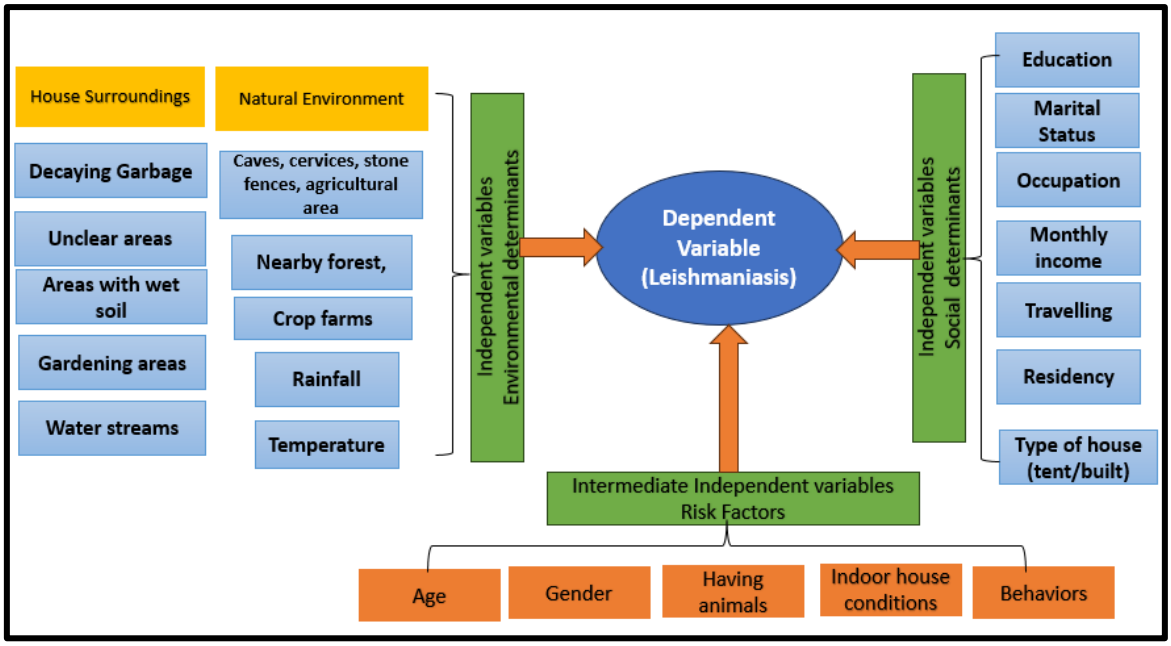

Figure 3.5: conceptual framework (Independent and dependent variables model) (prepared by researcher).

3.6.2. Validity of the questionnaire:

Validity of the questionnaire (internal consistency) was obtained through the study proposal defense session, (i.e., comments and suggestions came by the examiners). In addition,

questionnaire was reviewed by the supervisor and some modifications were adopted to be suitable for the Palestinian context.

The statistical validity of the questionnaire was assessed using Pearson's correlation test, which measured the correlation between the items of the questionnaire. The results indicated that the correlations were statistically significant, ranging from r=0.131 (p = 0.001) to r=0.538 (p = 0.000).

3.6.3 Piloting:

The questionnaire was piloted with 10 patients, in order to test it. These 10 patients were not included in the real study. Some questions or items were modified mainly related to type of house and staying place items.

3.7 Data collection procedure (fieldwork)

3.7.1. Ethical approval of the study:

All personal information of patients were anonymized. Permissions for conducting this study was obtained from the Ministry of Health (MOH) (Appendix 2) and the health department in each district in order to assess the patients' files and to get their contact information.

Consent form (Appendix 3) was signed by the participants showing the importance of the study, security and confidentiality of collected data and voluntary participation right of the participants.

Study design, research tools, and procedures had been approved by the ethical committee at Al-Quds University/Faculty of Public Health (Appendix 4).

3.7.2. Fieldwork:

Data on patients were collected from the Ministry of Health's Preventive Medicine Department. However, contacting patients proved challenging because many provided phone numbers were on Israeli networks, with some numbers being disconnected. As a result, the researcher and hired assistants visited the patients' homes after attempting phone contact to request interviews. Control subjects were selected from the same areas as the patients and were also asked to participate in interviews.

3.8 Data Analysis

Different statistical tests were used to analyze data including: descriptive analysis to explore distribution, frequencies, and percentages of participants and studied variables. Binary and multivariate regression and Chi-2 tests were used to assess and examine the association and relationship of variables to each other (pearson correlation and Odds Ratio (OR)). Statistical significance was at $p \leq 0.05$. Data treated and analyzed by using the Statistical Package for Social Sciences (SPSS IBM Statistics v.26).

CHAPTER FOUR: RESULTS

In this chapter, the researcher will present results and findings as outcomes of the study in relation to study questions and objectives.

4.1 The socio-demographic characteristics of the study sample

The following Table (4.1) presents description of the variables related to the study sample.

Table 4.1: Socio-demographic variables of cases and controls

	CONTROL N (%) *	CASE N (%)	Total N (%)
District			
Hebron	276 (44.4)	138 (22.2)	414 (66.7)
Bethlehem	138 (22.2)	69 (11.1)	207 (33.3)
Categories of age			
< 15 years	166 (26.7)	83 (13.4)	249 (40.1)
15-30 years	144 (23.2)	72 (11.6)	216 (34.8)
31-45 years	68 (11.0)	34 (5.5)	102 (16.4)
46-60 years	28 (4.5)	14 (2.3)	42 (6.8)
> 60 years	8 (1.3)	4 (0.6)	12 (1.9)
Gender			
Male	279 (44.9)	149 (24.0)	428 (68.9)
Female	135 (21.7)	58 (30.1)	193 (31.1)
Marital Status			
Married	189 (30.4)	77 (12.4)	266 (42.8)
Single	225 (36.2)	130 (20.9)	355 (57.2)
Education			
Basic school	322 (51.9)	196 (31.6)	518 (83.4)
University and college	79 (12.7)	11 (1.8)	90 (14.5)
Higher education	13 (2.1)	0.0	13 (2.1)
Main Occupation			
Farmer	24 (3.9)	59 (9.5)	83 (13.4)
Governmental servant	60 (9.7)	7 (1.1)	67 (10.8)
Laborer	187 (30.1)	46 (7.4)	233 (37.5)
Private sector employee	137 (22.1)	4 (0.6)	141 (22.7)
Self-employee	2 (0.3)	4 (0.6)	6 (1.0)
Household	2 (0.3)	14 (2.3)	16 (2.6)
Student	2 (0.3)	73 (11.8)	75 (12.1)
Residency place			
Rural area	414 (66.6)	187 (30.2)	601 (96.8)
Urban area	0.0 (0.0)	20 (3.2)	20 (3.2)
Monthly income			
≤1880 ILS	273 (44.0)	33 (5.3)	306 (49.3)
1880-4000 ILS	129 (20.8)	170 (27.4)	299 (48.1)
4001-6000 ILS	12 (1.9)	4 (0.6)	16 (2.6)
Travel to endemic area			
Yes	274 (44.1)	59 (9.5)	333 (53.6)
No	140 (22.5)	148 (23.8)	288 (46.4)
Total	**414**	**207**	**621**

**% = number/621*

Table (4.1) provides a detailed comparison of socio-demographic variables between cases and controls. The majority of participants resided in the Hebron district, representing 66.7% of the total sample, with a higher proportion among controls (44.4%) compared to cases (22.2%). Age distribution shows that younger individuals (< 15 years) were the most represented across both groups, accounting for 40.1% of the total, with 26.7% among controls and 13.4% among cases. Gender distribution indicates a predominance of males, who comprised 68.9% of the total sample. In terms of marital status, single participants were the largest group, making up 57.2% of the total. Education level shows that the majority had only basic schooling, especially among controls (51.9%). Occupational data reveals that laborers were the most common occupation among controls (30.1%), while a significant portion of cases were students (11.8%). Residency data highlights that almost all participants lived in rural areas, with very few from urban areas. Monthly income was generally low, with nearly half of the participants earning 1880 ILS or less. Finally, a notable portion of participants, particularly among controls (44.1%), reported traveling to endemic areas.

4.2 Distribution of Leishmaniasis by different factors

4.2.1. Frequency of Leishmaniasis by residence area:

Table 4.2: Distribution of leishmaniasis cases and controls among study sample by residence areas.

Residence area	Participants		Total
	Control	Case	
Dura	20 (4.8%)	10 (4.8%)	30 (4.8%)
Bani Na'im	54 (13.0%)	27 (13.0%)	81 (13.0%)
Taffuh	2 (0.5%)	1 (0.5%)	3 (0.5%)
Tarqumiya	4 (1.0%)	2 (1.0%)	6 (1.0%)
Idhna	4 (1.0%)	2 (1.0%)	6 (1.0%)
Yatta	136 (32.9%)	68 (32.9%)	204 (32.9%)
Sa'ir	18 (4.3%)	9 (4.3%)	27 (4.3%)
Za'tara	14 (3.4%)	7 (3.4%)	21 (3.4%)
Halhul	2 (0.5%)	1 (0.5%)	3 (0.5%)
Ar Rihiya	4 (1.0%)	2 (1.0%)	6 (1.0%)
Adh Dhahiriya	14 (3.4%)	7 (3.4%)	21 (3.4%)
Bethlehem	6 (1.4%)	3 (1.4%)	9 (1.4%)
Hebron	10 (2.4%)	5 (2.4%)	15 (2.4%)
A’rab ar Rashayida	114 (27.5%)	57 (27.5%)	171 (27.5%)
As Samu'	8 (1.9%)	4 (1.9%)	12 (1.9%)
Surif	4 (1.0%)	2 (1.0%)	6 (1.0%)
Total	**414 (66.7%)**	**207 (33.3%)**	**621 (100.0%)**

As mentioned in Table (4.2) residency data indicates that almost all participants lived in rural areas (96.8%) and (90.3%) out of the toral cases. The distribution presented in Table (4.1) is based on the results of the surveys conducted in the study and does not necessarily imply that there are no cases of leishmaniasis in other localities within Hebron Governorate, which comprises 97 communities, or Bethlehem Governorate, which includes 50 communities (PCBS

website). The data reflects the specific areas covered by the surveys and should not be interpreted as an exhaustive representation of all affected regions within these governorates. Table (4.2) illustrates the frequency of leishmaniasis cases and controls distributed by residence areas. The data reveals that the highest proportion of participants, both cases and controls, resided in Yatta, constituting 32.9% of the total sample. This is followed by participants from A'rab ar Rashayida, making up 27.5%. Bani Na'im also had a notable representation with 13.0% of participants. In contrast, areas like Taffuh, Halhul, and others had very low representation, each contributing 0.5% or 1.0% to the total sample. The distribution of cases and controls across the residence areas is consistent, with each area showing equal percentages for both groups. This uniformity suggests that the residence area may not be a significant differentiator between cases and controls in this sample.

4.2.2. Frequency of Leishmaniasis by Site of infection:

Table 4.3: Frequency of Site of infection in the body of Leishmaniasis patients (n=207)

Site of infection	Total	Male	Female
Hands	123 (59.4)	90 (43.4)	33 (15.9)
Legs	39 (18.8)	30 (14.4)	9 (4.3)
Neck	20 (9.7)	12 (5.7)	8 (3.8)
Face (below eyes and around mouth)	25 (12.1)	17 (8.2)	8 (3.8)
Total	**207**	**149**	**58**

Table (4.3) presents the distribution of leishmaniasis infection sites in the body among 207 patients, segmented by gender. The majority of patients were infected in their hands, affecting 59.4% of the patients. This includes 43.4% of males and 15.9% of females. The legs are the second most common site, with 18.8% of patients affected, comprising 14.4% of males and 4.3% of females. The neck is affected in 9.7% of the patients, with 5.7% being males and 3.8% females. Lastly, the face (specifically below the eyes and around the mouth) accounts for 12.1% of infections, with 8.2% in males and 3.8% in females.

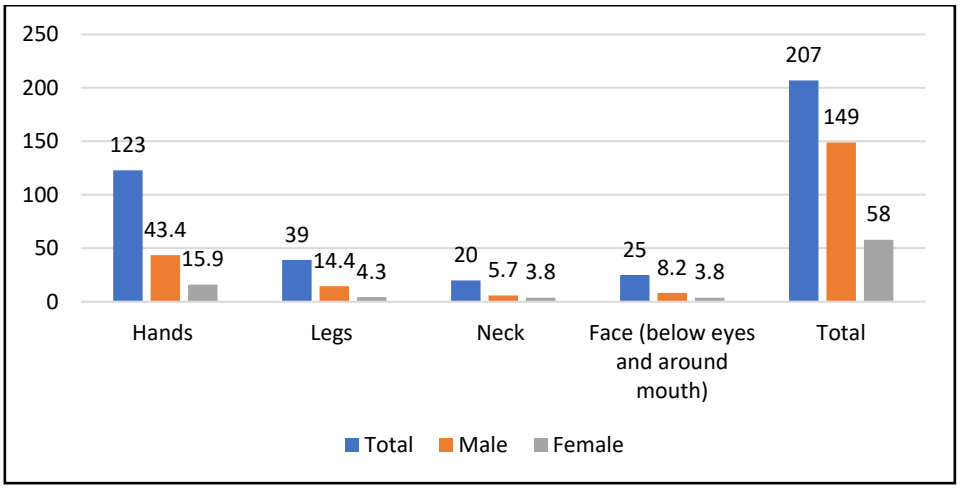

Figure 4.1: Distribution of Leishmaniasis infection sites by gender

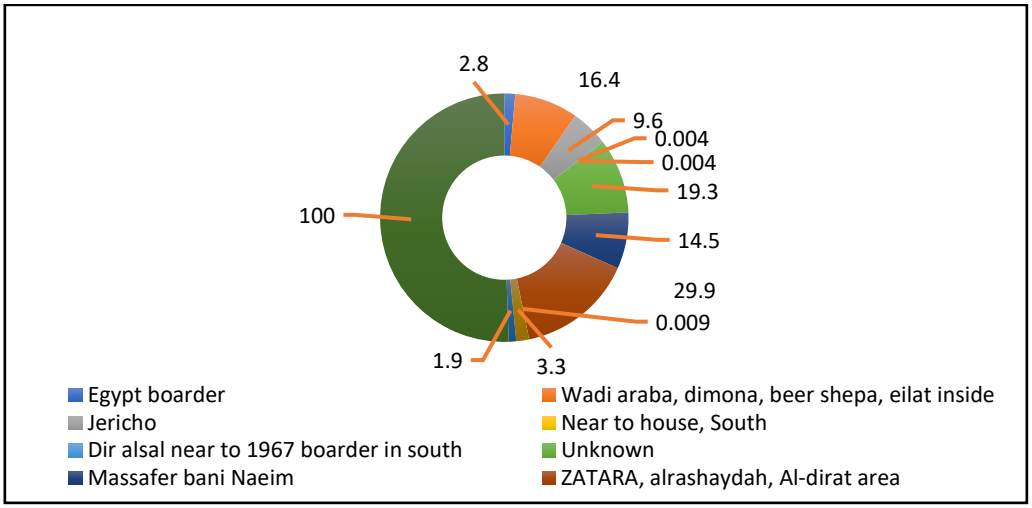

Figure (4.2): Source of Infection

The Graph (4.2) presents the distribution of leishmaniasis cases based on patients' responses to question about where you do you think got this infection. The majority of cases, accounting for 29.9%, were reported from the Za'tara, A'rab ar Rashayida, and Ad Deirat areas. This is followed by 19.3% of cases where the source was unknown. Other significant sources include Wadi Araba, Dimona, Beer Sheba, and Eilat inside Israel with 16.4%, and Masafer Bani Na'im with 14.5%. Jericho contributed 9.6% of the cases. Lesser sources include the Tel Aviv, Nazareth, and Asqalan areas (3.3%), Egypt border (2.8%), North Palestine including Nablus (1.9%), Julan Israel (0.009%), and near the house in the South (0.004%). Additionally, Deir al A'sal near the 1967 border in the South also accounted for 0.004% of the cases. Overall, a total of 207 cases were analyzed, reflecting a diverse geographic distribution of leishmaniasis sources.

4.2.3. Frequency of participants by the type of house:

Table 4.4: Frequency of participants (cases and controls) by type of house they live in

		Participants			Chi-square (sig.)*
		Control	Case	Total	
type of house	built house	348 (56.0%)	98 (15.8%)	446 (71.8%)	(91.9) 0.000
	tent	66 (10.6%)	109 (17.6%)	175 (28.2%)	
Total		414 (66.7%)	207 (33.3%)	621 (100.0%)	

**Chi-Square tests used*

Table (4.4) illustrates the frequency of participants (both cases and controls) by the type of house they reside in. The majority of participants, 71.8%, live in built houses, with 56.0% of these being controls and 15.8% being cases. In contrast, 28.2% of the participants live in tents, with a higher proportion of cases (17.6%) compared to controls (10.6%). The Chi-square test shows a significant difference in the distribution of participants by house type, with a p-value of 0.000,

indicating that the type of residence may be associated with the occurrence of leishmaniasis in this sample.

4.3 Risk factors for Leishmaniasis transmission

This section will present the potential effects or the relationships of different factors including socio-demographic factors, indoor and outdoor environment, and people's behavioral factors on the transmission of leishmaniasis.

4.3.1. Effect of social factors on leishmaniasis transmission:

Table 4.5: Binary regression analysis of Relationship[a] of Socio-demographic variables among cases and controls with leishmaniasis occurrence.

	Control (414) N (%)*	Case (207) N (%)	Total (621) N (%)	p-value
Categories of age				
< 15 years	166 (26.7)	83 (13.4)	249 (40.1)	0.662
15-30 years	144 (23.2)	72 (11.6)	216 (34.8)	0.445
31-45 years	68 (11.0)	34 (5.5)	102 (16.4)	0.349
46-60 years	28 (4.5)	14 (2.3)	42 (6.8)	0.350
> 60 years (ref.)	8 (1.3)	4 (0.6)	12 (1.9)	--
Gender				
Male	279 (44.9)	149 (24.0)	428 (68.9)	0.244
Female (ref.)	135 (21.7)	58 (30.1)	193 (31.1)	
Marital Status				
Married	189 (30.4)	77 (12.4)	266 (42.8)	0.045*
Single, divorced, widowed (ref.)	225 (36.2)	130 (20.9)	355 (57.2)	--
Education				
Basic school	322 (51.9)	196 (31.6)	518 (83.4)	< 0.001*
University and Higher education (ref.)	92 (14.8)	11 (1.8)	103 (16.6)	--
Main Occupation				
Farmer	24 (3.9)	59 (9.5)	83 (13.4)	< 0.001*
Governmental servant	60 (9.7)	7 (1.1)	67 (10.8)	< 0.001*
Laborer	187 (30.1)	46 (7.4)	233 (37.5)	< 0.001*
Private sector employee	137 (22.1)	4 (0.6)	141 (22.7)	< 0.001*
Self-employee	2 (0.3)	4 (0.6)	6 (1.0)	0.010*
Household	2 (0.3)	14 (2.3)	16 (2.6)	0.113
Student (ref.)	2 (0.3)	73 (11.8)	75 (12.1)	--
Residency place				
Rural	414 (66.6)	187 (30.2)	601 (96.8)	< 0.001*
Urban (ref.)	0.0 (0.0)	20 (3.2)	20 (3.2)	
Monthly income				
≤1880 ILS	273 (44.0)	33 (5.3)	306 (49.3)	0.094
1880-4000 ILS	129 (20.8)	170 (27.4)	299 (48.1)	0.020*
4001-6000 ILS (ref.)	12 (1.9)	4 (0.6)	16 (2.6)	--
Travel to endemic area				
Yes	274 (44.1)	59 (9.5)	333 (53.6)	< 0.001*
No (ref.)	140 (22.5)	148 (23.8)	288 (46.4)	--

[a] *Relation is significant at the $p \leq 0.05$ level*

**%=number/621*

Table (4.5) illustrates that the socio-demographic variables show varied relationships with leishmaniasis occurrence among cases and controls. Age categories also show no significant association with the disease (p-values between 0.349 and 0.662), suggesting that age is not a strong risk factor in this sample. Gender does not appear to significantly affect leishmaniasis occurrence (p-value = 0.244), with a higher proportion of males in both cases and controls. Marital status is a notable factor, with married individuals being less represented among cases (12.4%) compared to controls (30.4%), indicating a potential protective effect (p-value = 0.045).

Education level shows a strong association, with individuals having only basic school education being more prevalent among cases (31.6%) compared to controls (51.9%), highlighting education as a significant risk factor (p-value < 0.001). Main occupation is also a significant factor, with farmers, governmental servants, laborers, and private sector employees showing a higher prevalence among cases compared to controls (p-values < 0.001). Residency in rural areas is strongly associated with leishmaniasis, as evidenced by the higher proportion of rural residents among cases (30.2%) compared to controls (66.6%) (p-value < 0.001). Monthly income and travel to endemic areas also play roles, with significant differences observed in income brackets (p-value = 0.020) and a higher occurrence among those who travel to endemic areas (*if he/she had been in Jericho as an example*) (p-value < 0.001).

4.3.2. Effect of Environmental factors on leishmaniasis transmission:

4.3.2.1. House Surroundings:

In the investigation of environmental factors associated with leishmaniasis occurrence, a series of statistical analyses were conducted to evaluate the impact of various environmental conditions. The primary aim was to discern how factors such as decaying garbage, unclear areas, unclean areas, areas with wet soil, gardening areas, and water streams influence the likelihood of leishmaniasis.

The analysis utilized chi-square tests to assess the association between each environmental factor and the occurrence of leishmaniasis. Chi-square tests are well-suited for this purpose as they determine whether there is a significant difference between observed and expected frequencies in categorical data. This test provides a measure of how likely it is that an observed distribution is due to chance, and it is particularly useful for understanding relationships between categorical variables.

Table 4.6: Distribution of leishmaniasis cases and controls by house outdoor surroundings*

	Control N (%)	Case N (%)	Total N (%)	Chi - square value	Odds Ratio (OR) (95% CI	p-value
Decaying Garbage						
Present	197 (31.7)	54 (8.7)	251 (40.4)	2.572	1.8 (1.4-2.3)	< 0.001
Absent (ref.)	217 (52.4)	153 (24.6)	370 (59.6)		0.709 (0.627-0.801)	
Unclean areas						
Present	63 (10.1)	184 (29.6)	247 (39.8)	312.675	7.6 (5.1-11.2)	< 0.001
Absent (ref.)	351(56.6)	23(3.7)	374 (60.2)		0.171 (0.136-0.216)	
Areas with wet soil						
Present	2 (0.3)	54 (8.7)	56 (9.0)	110.265	1.3 (1.2-1.4)	< 0.001
Absent (ref.)	412 (66.3)	153 (24.6)	565 (91.0)		0.019 (0.005-0.075)	
Gardening areas						
Present	208 (33.5)	119 (19.2)	327 (52.7)	2.907	0.874 (0.751-1.017)	0.088
Absent (ref.)	206 (33.2)	87 (14.0)	293 (47.2)		1.2 (0.972-1.409)	
Water Streams						
Present	18 (2.9)	94 (15.6)	115 (18.5)	165.287	1.8 (1.5-2.0)	< 0.001
Absent (ref.)	396(63.8)	110 (17.7)	506 (81.5)		0.093 (0.058-0.149)	

**Chi-Square tests used*

Table (4.6) illustrates the relationship between various outdoor surroundings and the occurrence of leishmaniasis cases compared to controls.

Decaying garbage: The analysis of the relationship between decaying garbage and leishmaniasis occurrence reveals a statistically significant association. The odds ratio for leishmaniasis occurrence is 2.572 ($p < 0.001$), indicating that individuals with leishmaniasis are more likely to be exposed to decaying garbage compared to controls. Specifically, the presence of decaying garbage is associated with an increased risk of leishmaniasis (odds ratio = 1.824, 95% CI: 1.420 - 2.344), while the absence of decaying garbage is associated with a decreased risk (odds ratio = 0.709, 95% CI: 0.627 - 0.801).

Unclean area: results in table 4.6 illustrates a strong association between the presence of unclean areas and leishmaniasis occurrence. The Pearson Chi-Square statistic of 312.675 ($p < 0.001$) indicates a highly significant relationship, which is further supported by the Likelihood Ratio and Fisher's Exact Test, both showing p-values of 0.000.

The odds ratio for leishmaniasis in the presence of unclean areas is 7.630 (95% CI: 5.179 - 11.241), signifying that individuals in environments with unclean areas are significantly more likely to develop leishmaniasis. Conversely, the odds ratio for leishmaniasis in the absence of unclean areas is 0.171 (95% CI: 0.136 - 0.216), indicating a much lower risk of leishmaniasis.

Areas with wet soil: results present the association between the presence of wet soil and the occurrence of leishmaniasis. The Pearson Chi-Square value of 110.265 ($p < 0.001$), along with the significant results from the Likelihood Ratio and Fisher's Exact Test, indicates a highly significant relationship.

The odds ratio for leishmaniasis in areas with wet soil is 1.346 (95% CI: 1.241 - 1.460), suggesting a higher likelihood of the disease in these areas. compared to those without wet soil. In contrast, the odds ratio for leishmaniasis in areas without wet soil is 0.019 (95% CI: 0.005 - 0.075), demonstrating a significantly lower likelihood of leishmaniasis in such environments

Gardening areas: In contrast, gardening areas do not show a significant association with the occurrence of leishmaniasis, with 19.2% of cases and 33.5% of controls residing in such areas (p-value = 0.088). This suggests that while gardening areas variable is common, it does not have any impact on the disease spreading. The results are consistent across other statistical tests, including the Likelihood Ratio and Fisher's Exact Test.

The odds ratio for leishmaniasis in gardening areas is 0.874 (95% CI: 0.751 - 1.017), indicating a slightly lower likelihood of the disease in such areas, though this association is not statistically significant. Conversely, the odds ratio for areas without gardening is 1.170 (95% CI: 0.972 - 1.409), suggesting a slightly higher likelihood of leishmaniasis in these areas, but again, this finding is not statistically significant.

Water streams: presents the relationship between the presence of water streams and the occurrence of leishmaniasis. The Chi-Square tests reveal a highly significant association (Pearson Chi-Square = 165.287, $p < 0.001$) between the presence of water streams and leishmaniasis cases.
The odds ratio for leishmaniasis in areas with water stream is 1.8 (95% CI: 1.5 - 2.0), suggesting a higher likelihood of the disease in these areas. compared to those without water stream. (p-value < 0.001).

4.3.2.2. House location:

Table 4.7: Results of Chi-square test for the association between transmission of leishmaniasis and house location in residence area

	Control N (%)	Case N (%)	Total N (%)	Chi - square value	OR	p-value (0.05)
Location of the house						
Center of the domestic area	350 (56.4)	7 (1.1)	357 (57.5)	371.936	25.0 (12.05-51.84)	< 0.001
Peripheral of the domestic area	64 (10.3)	200 (32.2)	264 (42.5)		156.2 (70.2-347.5)	
Total	414	207				

Table (4.7) presents the results of the analysis examining the association between the location of the house and leishmaniasis occurrence. The data show a significant relationship between house location and the likelihood of leishmaniasis. Specifically, individuals residing in the center of the domestic area were far less likely to contract leishmaniasis, with only 7 cases (1.1%) compared to 350 controls (56.4%) in this area. In contrast, a substantial proportion of leishmaniasis cases, 200 (32.2%), lived in the peripheral areas, while only 64 controls (10.3%) resided in these areas.

The chi-square test yielded a value of 371.936 with a p-value of <0.001, indicating a highly significant association between house location and leishmaniasis occurrence. This result is further supported by the likelihood ratio and Fisher's Exact Test, both of which also indicate statistical significance. The odds ratio analysis reveals an exceptionally high likelihood of leishmaniasis for those living in peripheral areas, with an odds ratio of 156.250, suggesting that residents of these areas are at a markedly increased risk compared to those living in the center of the domestic area.

4.3.2.3 House condition status vs. leishmaniasis occurrence:

Table 4.8: Results of Multinomial Logistic Regression Analysis for the Association between House Condition and Leishmaniasis Occurrence

	Control N (%)	Case N (%)	Total N (%)	OR	p-value
House conditions					
Poor	3 (0.5)	57 (9.2)	60 (9.7)	0.091 (0.027-0.303)	< 0.001
Moderate	340 (54.8)	23 (3.7)	363 (58.5)	25.576 (15.14-43.19)	< 0.001
Good	8 (1.3)	18 (2.9)	26 (4.2)	0.769 (0.316-1.870)	0.562
Living in tents (ref.)	63 (10.1)	109 (17.6)	172 (27.7)	---	

The analysis explores the relationship between house condition and the occurrence of leishmaniasis.

The model fitting information indicates that the model, including house condition as a predictor, significantly fits the data ($p < 0.001$). The likelihood ratio tests show that the inclusion of house condition in the model explains a significant portion of the variability in leishmaniasis occurrence (Chi-Square = 337.222, $p < 0.001$). The parameter estimates suggest the following:

Poor House Condition: Residents living in poor house conditions are significantly less likely to be controls (i.e., they are more likely to have leishmaniasis), with an odds ratio of 0.091 (95% CI: 0.027 – 0.303).

Moderate House Condition: Residents in moderately conditioned houses have a significantly higher likelihood of being controls, with an odds ratio of 25.576 (95% CI: 15.145 – 43.191), indicating a protective effect against leishmaniasis.

Good House Condition: This category does not show a statistically significant effect, with an odds ratio close to 1, indicating no strong association with leishmaniasis occurrence (p=0.562).

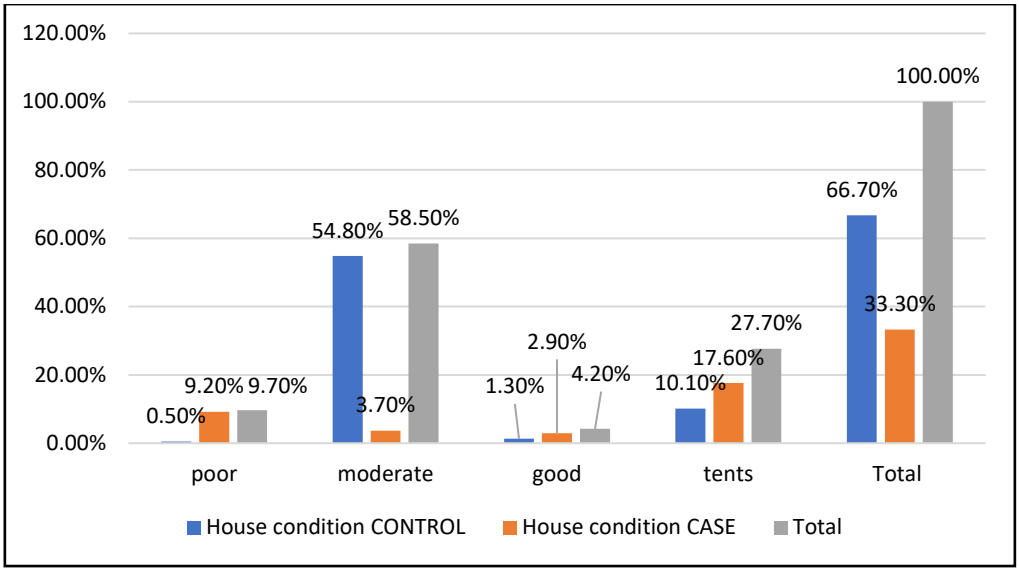

Figure 4.3: Distribution of cases and controls by house condition level

The Figure (4.3) highlights a strong association between poor housing conditions and higher leishmaniasis cases. Conversely, moderate housing conditions are more common among the control group, indicating a lower risk. The data suggests that improving housing conditions could be a key factor in reducing leishmaniasis incidence.

4.3.2.4. House family occupancy:

Table 4.9: Chi-Square Test Results and Logistic Regression Analysis for the Effect of Household Crowding on Leishmaniasis Occurrence

Variable	Chi -Square	(OR)	Sig.	95% CI
Persons per house	22.7			
1-5		2.118	<0.001	(1.516, 2.959)
>5		0.780		(0.711, 0.856)
Variable	**Chi -Square**	**Exp(B) (OR)**	**Sig.**	**95% CI for Exp(B)**
Persons per bedroom				
One or two	-4.505	0.011	0.000	(0.004, 0.028)
Three or more	0.892	2.440	0.002	(1.370, 4.347)
No room / tent	0.489	1.631	0.004	(1.158, 2.298)

The Chi-Square test results indicate a significant association between household crowding and the occurrence of leishmaniasis. Households with more than five persons per house are at a higher risk, with an odds ratio (OR) of 0.780 (95% CI: 0.711, 0.856, $p < 0.001$), suggesting a lower likelihood of remaining disease-free compared to those with 1-5 persons per house, which have an OR of 2.118 (95% CI: 1.516, 2.959, $p < 0.001$). This result highlights that smaller household sizes are associated with a reduced risk of leishmaniasis.

Logistic regression analysis further underscores the role of bedroom crowding in leishmaniasis risk. Households with three or more persons per bedroom have a significantly increased likelihood of leishmaniasis, with an OR of 2.440 (95% CI: 1.370, 4.347, p = 0.002). Conversely, households with one or two persons per bedroom have a drastically lower risk, evidenced by an OR of 0.011 (95% CI: 0.004, 0.028, p < 0.001). Additionally, those living in tents or with no defined rooms have an OR of 1.631 (95% CI: 1.158, 2.298, p = 0.004). **4.3.2.5 House internal structure and conditions:**

Table 4.10: Logistic Regression Analysis of House indoor and outdoor characteristics in relation to the leishmaniasis occurrence

	Control N (%)	**Case N (%)**	**Total N (%)**	**Exp (OR)**	**p-value (0.05)**	95% CI for Exp(B):
Type of house						
Instruction Built	348 (84.1)	98 (47.3)	446 (71.8)	5.86	0.000	.014-8.5
Tent ***(ref.)***	66 (15.9)	109 (52.7)	175 (28.2)			
Type of wall covering						
Unplaster/ normal paint	64 (15.5)	46 (22.2)	110 (17.7)	2.96	0.000	1.8-4.8
Plastered / oily paint	132 (31.9)	4 (1.9)	136 (21.9)	70.3	0.000	24.8-199.0
Mixed	157 (37.9)	27 (13.0)	184 (29.6)	12.3	0.000	7.4-20.6
Tent ***(ref.)***	61 (14.7)	130 (62.8)	191 (30.8)			
Structure of housing						
Underground	121 (29.2)	15 (7.2)	136 (21.9)	13.3	0.000	7.1-24.7
One floor	71 (17.2)	53 (25.6)	124 (20.0)	2.21	0.001	1.3-3.5
Multi-floors	156 (37.7)	30 (14,5)	186 (30.0)	8.58	0.000	5.2-14.1
Tent ***(ref.)***	66(15.9)	109 (62.3)	175 (28.2)			
Staying Place						
In first floor	296(71.5)	72 (34.8)	368 (59.3)	6.73	0.000	4.5-9.9
In upper floor	49 (11.8)	22 (10.6)	71 (11.4)	3.64	0.000	2.0-6.5
Tent ***(ref.)***	69 (16.7)	113 (54.6)	182 (29.3)			
Living in a house with cracked wall						
Yes	0 (0.0)	51 (24.6)	51 (8.2)	0.03	0.001	0.004- 0.234
No	348 (84.1)	47 (22.7)	395 (63.6)	11.6	<0.001	7.5-17.8
Tent ***(ref.)***	66 (15.9)	109 (52.7)	175 (28.2)			
Living in a house with cracked floors						
Yes	2 (0.5)	49 (23.7)	51 (8.2)	0.06	<0.001	0.016- 0.290
No	348 (84.1)	51 (24.6)	399 (64.3)	11.4	<0.001	7.4-17.4
Tent ***(ref.)***	64 (15.5)	107 (51.7)	171 (27.5)			
Window of the house						
With net	230 (55.61)	34 (16.4)	264 (42.5)	11.3	<0.001	7.0-18.1
Without net	120 (29.0)	66 (31.9)	186 (30.0)	3.04	<0.001	1.9-4.6
Tent ***(ref.)***	64 (15.5)	107 (51.7)	171 (27.5)			
Materials in the yards						
Stones	1 (0.2)	15 (2.4)	16 (2.6)	0.06	0.060	0.004-1.11
leaves, and tree trunk	0.0 (0.0)	7 (1.1)	7 (1.1)	0.14	0.184	0.008-2.51
Both	410 (66.0)	183 (29.5)	593 (95.5)	2.24	0.422	0.313-16.0
Empty area/desert ***(ref.)***	3 (0.5)	2 (0.3)	5 (0.8)			
Sanitation						
Inadequate access to sanitation	65 (10.5)	157 (25.3)	222 (35.7)	0.05	0.000	0.039-0.090
Adequate access to sanitation ***(ref.)***	349 (56.2)	50 (8.1)	399 (64.3)			
Sewage system/waste management						
Present	77 (12.4)	52 (8.4)	129 (20.8)	0.68	0.060	0.457-1.016
Absent ***(ref.)***	337 (54.3)	155 (25.0)	492 (79.0)			

Table (4.10) shows the significant effects of various house characteristics on the likelihood of contracting leishmaniasis.

Type of House: The odds of contracting leishmaniasis are significantly lower for those living in instruction-built houses compared to tents (OR: 5.865, $p < 0.001$). This suggests that well-constructed houses offer a strong protective effect against leishmaniasis.

Type of Wall Covering: The type of wall covering significantly influences leishmaniasis risk. Houses with plastered/oily paint (OR: 70.328, $p < 0.001$) or mixed wall coverings (OR: 12.392, $p < 0.001$) have higher odds of leishmaniasis compared to those with un-plastered/normal paint. This indicates that certain wall types are associated with an increased risk of the disease.

Structure of Housing: The structure of the house also plays a crucial role. Underground houses have significantly higher odds of leishmaniasis (OR: 13.322, $p < 0.001$), while multi-floor structures (OR: 8.588, $p < 0.001$) and single-floor houses (OR: 2.212, $p = 0.001$) show varying levels of risk compared to tents.

Staying Place: Residents staying on the first floor are significantly less likely to contract leishmaniasis (OR: 6.733, $p < 0.001$), and those on upper floors also show reduced risk (OR: 3.648, $p < 0.001$) compared to those staying in tents.

Living in a House with Cracked Walls: Living in a house with cracked walls is strongly associated with higher odds of leishmaniasis (OR: 0.032, $p < 0.001$), while intact walls are associated with lower risk (OR: 11.619, $p < 0.001$).

Living in a House with Cracked Floors: Similar to cracked walls, cracked floors are linked with increased leishmaniasis risk (OR: 0.068, $p < 0.001$). Houses with intact floors have a significantly lower risk (OR: 11.408, $p < 0.001$).

Window of the House: Houses with netted windows are significantly less likely to have leishmaniasis (OR: 11.310, $p < 0.001$). Houses without nets also show a reduced risk (OR: 3.040, $p < 0.001$).

Materials in the Yards: The presence of materials like stones or leaves in the yard does not show a significant impact on leishmaniasis risk (ORs ranging from 0.067 to 2.240, with varying p-values).

Sanitation: Inadequate access to sanitation is associated with significantly higher odds of leishmaniasis (OR: 0.059, $p < 0.001$). Adequate sanitation is strongly protective against the disease.

Sewage System/Waste Management: The presence of a sewage system shows a marginally significant effect on leishmaniasis risk (OR: 0.681, $p = 0.060$), indicating a possible protective effect, though not statistically significant at the conventional 0.05 level.

Overall, the results emphasize that both structural and sanitation-related factors play significant roles in the risk of contracting leishmaniasis, with well-maintained and adequately equipped houses providing substantial protection against the disease.

4.2.3. Effect of having animals on leishmaniasis transmission:

Table 4.11: Results of Chi-square test for relationship between animals Ownership and Leishmaniasis Occurrence

	Control N (%)	Case N (%)	Total N (%)	Pearson Chi-Square	Odds Ratio (OR) (95% CI	p-value Fisher test
Having animals				**6230, p < 0.001**		
No (ref,)	354 (57.0)	12 (1.9)	366 (58.9)		**14.7** (8.50-25.54)	**< 0.001**
Yes	60 (9.7)	195 (31.4)	255 (41.1)			
Dogs				**13.51, p < 0.001**		
No (ref.)	84 (13.5)	18 (2.9)	102 (16.4)		**2.6** (1.558 - 4.584)	**0.012**
Yes	330(53.1)	189 (30.4)	519 (83.6)			
Cats				**13.80, p < 0.001**		
No (ref.)	137 (22.1)	39 (6.3)	176 (28.3)		**2.1** (1.422 - 3.191)	**0.014**
Yes	277 (44.6)	168 (27.1)	445 (71.7)			
Cattle, sheep, goats, cows				**0.074, p = 0.785**		
No (ref.)	94 (15.1)	45 (7.2)	139 (22.4)		**1.05** (0.707 - 1.581)	0.435
Yes	320 (51.5)	162 (26.1)	482 (77.6)			
Chicken				**15.8, p = 0.000**		
No (ref.)	84 (13.5)	73(11.8)	157 (25.3)		**1.231** (1.101-1.377)	**< 0.001**
Yes	330 (53.1)	134 (21.6)	464 (74.7)			
Rodents and rats				**200.1, p = 0.000**		
No (ref.)	408 (65.7)	112 (18.0)	520 (83.7)		**57.6** (24.67-135.09)	**< 0.001**
Yes	6 (1.0)	95 (15.3)	101 (16.3)			
Hens				**1.819, p = 0.177**		
No (ref.)	278 (44.8)	150 (24.2)	428 (68.9)		**1.193** (0.919-1.548)	0.104
Yes	136 (21.9)	57 (9.2)	193 (31.1)			
Rocky hyrax				**146.1, p = 0.000**		
No (ref.)	364 (58.6)	87 (14.0)	451 (72.6)		**10.04** (6.70-15.04)	**< 0.001**
Yes	50 (8.1)	120 (19.3)	170 (27.4)			
Foxes				**4.624, p = 0.032**		
No (ref.)	412 (66.3)	202 (32.5)	614 (98.9)		**5.09** (0.98-26.50)	**0.044**
Yes	2 (0.3)	5 (0.8)	7 (1.1)			

From the Table (4.11), we can see the effect of owning animals on leishmaniasis occurrence. The chi-square test results highlight the varying degrees of association between different types of animal ownership and the likelihood of contracting leishmaniasis.

Overall Animal Ownership:

The presence of animals around the home is strongly associated with leishmaniasis (Pearson Chi-Square = 6230, $p < 0.001$). The odds of contracting leishmaniasis are significantly higher in households with animals, with an odds ratio of 14.7 (95% CI: 8.50–25.54), indicating a substantial risk increase.

Dogs: Owning dogs is significantly linked to a higher risk of leishmaniasis (Pearson Chi-Square = 13.51, $p < 0.001$). Households with dogs have an odds ratio of 2.6 (95% CI: 1.558–4.584), suggesting that the presence of dogs more than doubles the risk of leishmaniasis.

Cats: The presence of cats also shows a significant association with leishmaniasis (Pearson Chi-Square = 13.80, $p < 0.001$). The odds ratio is 2.1 (95% CI: 1.422–3.191), indicating that individuals in households with cats have more than twice the risk of contracting leishmaniasis compared to those without cats.

Cattle, Sheep, Goats, Cows: Ownership of cattle, sheep, goats, or cows does not show a significant association with leishmaniasis (Pearson Chi-Square = 0.074, $p = 0.785$). The odds ratio of 1.05 (95% CI: 0.707–1.581) suggests that these animals do not meaningfully affect the risk of leishmaniasis.

Chicken: Having chickens is associated with an increased risk of leishmaniasis (Pearson Chi-Square = 15.8, $p < 0.001$). The odds ratio is 1.231 (95% CI: 1.101–1.377), indicating a modest increase in risk for those with chickens compared to those without.

Rodents and Rats: The presence of rodents and rats around the home is strongly linked to a higher risk of leishmaniasis (Pearson Chi-Square = 200.1, $p < 0.001$). The odds ratio of 57.6 (95% CI: 24.67–135.09) demonstrates a very high risk associated with these animals.

Hens: Ownership of hens does not show a significant association with leishmaniasis (Pearson Chi-Square = 1.819, $p = 0.177$). The odds ratio is 1.193 (95% CI: 0.919–1.548), indicating no significant increase in risk.

Rocky Hyrax: The presence of rocky hyraxes is significantly associated with leishmaniasis (Pearson Chi-Square = 146.1, $p < 0.001$). The odds ratio of 10.04 (95% CI: 6.70–15.04) suggests a strong association, with a high risk of leishmaniasis for those exposed to rocky hyraxes.

Foxes: The association between foxes and leishmaniasis is significant (Pearson Chi-Square = 4.624, $p = 0.032$). The odds ratio of 5.09 (95% CI: 0.98–26.50) indicates a higher risk of leishmaniasis in households with foxes, though the risk is less pronounced compared to some other animals.

Overall, these results underscore the significant impact that various types of animal ownership can have on the risk of leishmaniasis, with some animals showing a particularly strong association with the disease.

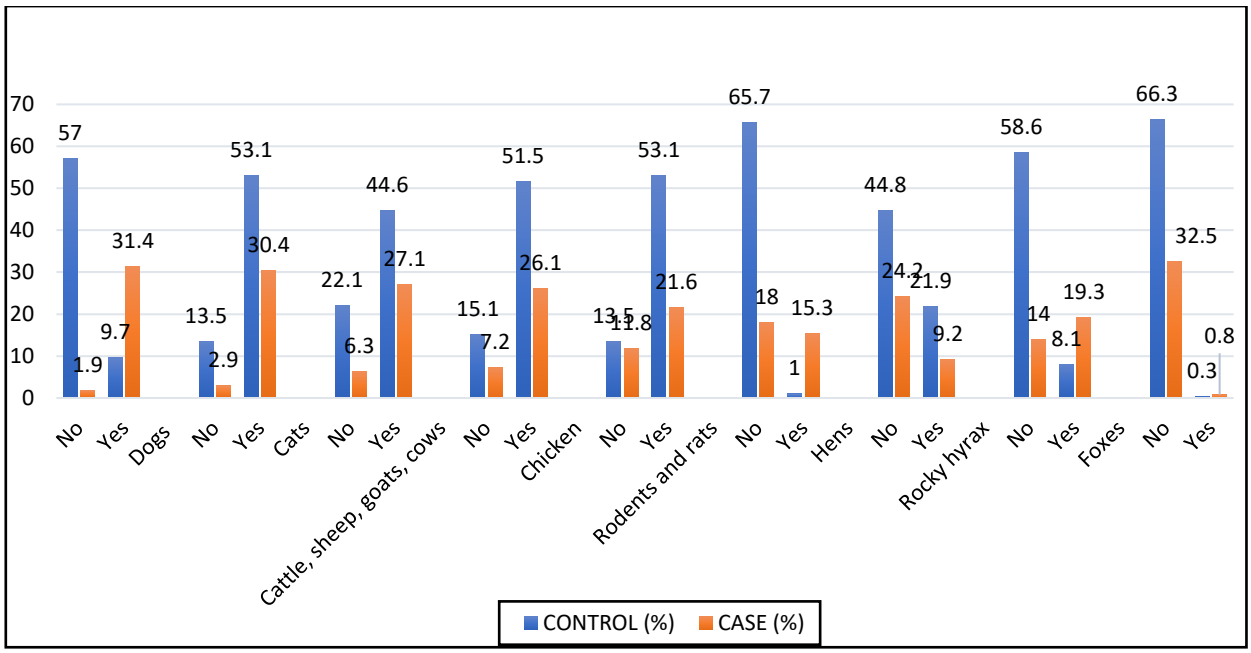

Figure 4.4: Distribution and percentages of animals owned or frequently visiting home/ near or around house

Figure (4.4) shown the presence of rodents, rats, rocky hyrax, and particularly foxes, shows a higher prevalence in leishmaniasis cases, highlighting a potential linkage between these animals and the transmission of the infection.

4.2.4. Topography and Climate risk factors:

In this section, we explore the relationship between leishmaniasis occurrence and various topographical and climate-related factors in the study area, providing insights into how these environmental conditions contribute to the disease's occurrence and distribution

Table 4.12: Distribution of leishmaniasis cases and controls by residence area topography and climate risk factors

	Control N (%)	Case N (%)	Total N (%)	p-value Fisher test
Natural environment				
Caves, Crevices, Stone fences	2 (0.3)	174 (28.0)	176 (28.3)	< 0.001
Agricultural area	62 (10.0)	29 (4.7)	91 (14.7)	
Urban Area	350 (56.4)	4 (0.6)	354 (57.6)	
Rainfall				
<the average/year	293 (47.2)	65 (10.5)	358 (57.6)	< 0.001
=the average/year	121 (19.5)	139 (22.4)	260 (41.9)	
>the average/year	0.0 (0.0)	3 (0.5)	3 (0.5)	
Temperature				
Average minimum temperature /month	0.0 (0.0)	3 (0.5)	3 (0.5)	< 0.001
Average maximum temperature/ month	295 (47.5)	114 (18.4)	409 (65.9)	
Average medium temperature /month	119 (19.2)	90 (14.5)	209 (33.7)	

Table (4.12) displays the Logistic Regression Analysis analysis of leishmaniasis cases and controls by residence area topography and climate risk factors reveals significant associations that can inform public health strategies. Living near natural environments such as caves, crevices, and stone fences are linked to higher risk of leishmaniasis, as evidenced by 28.0% of cases compared to only 0.3% of controls in these areas ($p < 0.001$). This suggests that such environments are conducive to the habitats of sandflies, the disease vectors. Conversely, urban areas, which host a majority of controls (56.4%) but very few cases (0.6%), are associated with a significantly lower risk, likely due to fewer vector habitats and better living conditions.

Agricultural areas show a moderate presence of cases (4.7%) and controls (10.0%), indicating some level of risk related to farming activities and exposure to vectors.

Climate factors further influence disease risk. Areas with below-average rainfall have a significantly higher proportion of cases (10.5%) compared to controls (47.2%), indicating that drier conditions might favor vector activity and disease transmission ($p < 0.001$). In contrast, areas with rainfall equal to the annual average show moderate risk, while those with above-average rainfall have minimal cases, suggesting less favorable conditions for vector proliferation.

Temperature analysis indicates that both minimum and medium temperatures are associated with leishmaniasis cases (0.5% and 14.5%, respectively), although the distribution of controls suggests that extreme temperatures might limit vector activity. The odds ratio for average monthly minimum temperature (1.3; 95% CI: 1.2-1.4) further highlights temperature as a risk factor. Findings shown the necessity of considering environmental and climatic determinants in leishmaniasis prevention and control, particularly in managing vector habitats and targeting high-risk areas.

4.2.4.1. Rainfall in Palestine (2014-2023):

Data on annual rainfall from 2014 to 2023 obtained by referring to the Palestinian Meteorological Authority *(www.pmd.ps/en/)* and by a personal communication with people working in the authority office. These data were analyzed in relation to the leishmaniasis occurred during that period. Table 4.13 below shows the association between Rainfall and disease occurrence.

Table 4.13: Association between annual rainfall on leishmaniasis in Hebron and Bethlehem Districts

	2014		2015		2016		2017		2018		2019		2020		2021		2022		2023		**p-value**
	CL	VL	CL	VL	CL	VL	CL	VL	CL	VL	CL	VL	CL	VL	CL	VL	CL	VL	CL	VL	
Hebron	46	0	32	3	30	3	33	1	46	1	6	1	16	2	19	1	23	0	21	2	**0.764**
Annual Rainfall	444.8		511.7		553.4		243.4		518		394.1		757.4		362.2		496		493.2		
Bethlehem	18	0	11	0	6	0	6	1	13	1	1	10	0	0	6	0	3	0	10	0	**0.270**
Annual Rainfall	378.8		542.9		605.6		355.7		621		495.1		702.5		442.5		512.2		464.5		

Table (4.13) displays regression analysis of the association between annual rainfall and the infection occurrence likelihood in the Hebron and Bethlehem districts over a ten-year period from 2014 to 2023. The table categorizes cases into cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL), showing the annual case counts for each type in both districts, along with the annual rainfall data.

In Hebron, cutaneous leishmaniasis cases vary each year, with a peak of 46 cases in 2014 and 2018, and a low of 6 cases in 2019. Visceral leishmaniasis cases are consistently low, ranging from 0 to 3 cases per year. The annual rainfall in Hebron fluctuates significantly, from a low of 243.4 mm in 2017 to a high of 757.4 mm in 2020. The p-value for the association between annual rainfall and leishmaniasis incidence in Hebron is 0.764, indicating no statistically significant correlation.

In Bethlehem, cutaneous leishmaniasis cases are generally lower than in Hebron, with a peak of 18 cases in 2014 and a minimum of 0 cases in 2020. Visceral leishmaniasis cases are rare, with only occasional occurrences (maximum of 1 case in a year). The annual rainfall in Bethlehem also shows variation, ranging from 355.7 mm in 2017 to 702.5 mm in 2020. The p-value for the association between annual rainfall and leishmaniasis incidence in Bethlehem is 0.270, also indicating no statistically significant correlation.

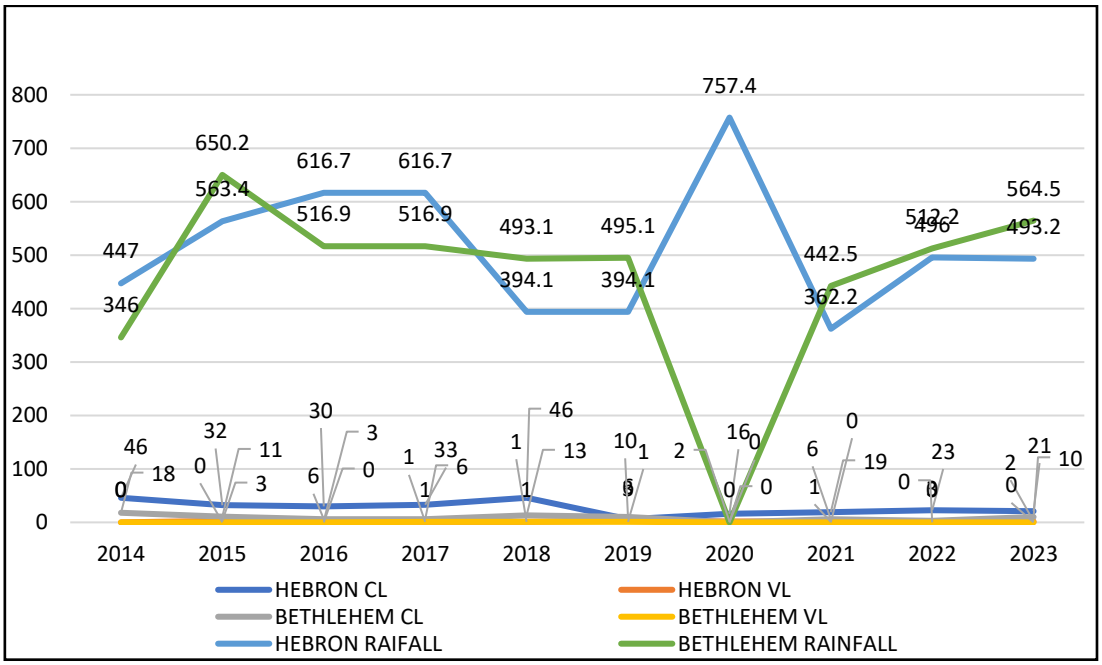

Figure 4.5: Annual rainfall (2014-2023) with leishmaniasis cases in Hebron and Bethlehem Districts

4.2.5. Awareness about the disease:

Table 4.14: Distribution of leishmaniasis cases and controls by their knowledge

	Control N (%)	Case N (%)	Total N (%)	R (Pearson correlation)
Heard about disease (before infection)				
Yes	350 (56.4)	108 (17.4)	458 (73.8)	.347 (0.000)
No	64 (10.3)	99 (47.8)	163 (26.2)	
Family knowledge of the vector				
Yes	352 (56.7)	145 (23.3)	497 (80.0)	.177 (0.000)
No	62 (10.0)	62 (10.0)	124 (20.0)	

The analysis of leishmaniasis cases and controls by their knowledge about the disease reveals significant insights into the importance of awareness and family knowledge in disease prevention. A substantial majority of controls (56.4%) had heard about leishmaniasis before infection, compared to only 17.4% of cases.

Furthermore, family knowledge of the vector is prevalent among controls (56.7%) compared to cases (23.3%), indicating that understanding the vector's behavior and habitats can lead to better preventive practices and reduced risk of infection. The equal distribution of controls and cases (both 10.0%) with no family knowledge suggests that increasing family knowledge might further enhance protective behaviors and reduce disease incidence. These findings emphasize the significant role of disease awareness and family knowledge in preventing leishmaniasis, advocating for comprehensive public health education initiatives to improve awareness and understanding of the disease and its vectors.

Overall, the data suggests that having prior knowledge about the disease and family knowledge of the vector are both significantly associated with lower rates of leishmaniasis infection. The stronger correlation for hearing about the disease indicates it may play a more critical role in preventing infection.

4.3 Source of information

Figure (4.6) illustrates the distribution of participants' percentages by their sources of knowledge about leishmaniasis. The majority of participants (48%) reported that TV/Radio was their primary source of information. Health workers were the second most common source, informing 29% of participants. Friends contributed to 19% of the knowledge dissemination among participants, while printed media accounted for a minimal 1%.

This distribution highlights the critical role of mass media, particularly TV and radio, in raising awareness about leishmaniasis. The significant contribution of health workers underscores the importance of medical professionals in public health education. Conversely, the low percentage of participants informed through printed media suggests that traditional print sources are less effective in reaching the population regarding this health issue. Overall, these findings suggest

that leveraging TV, radio, and healthcare providers could be the most effective strategy for disseminating information about leishmaniasis to the community.

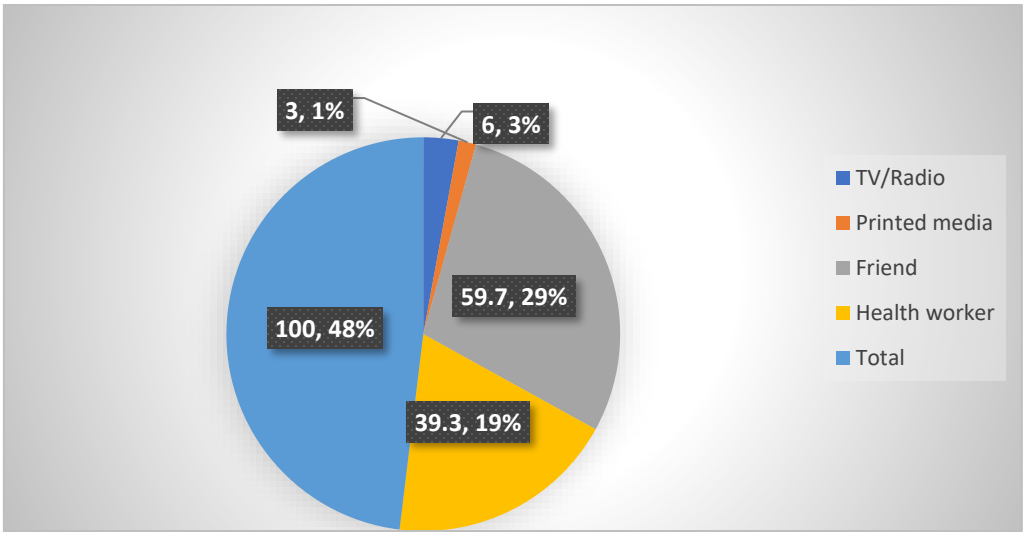

Figure 4.6: Distribution of participants percentages by source of knowledge about Leishmaniasis

4.4 Behavioral characteristics and prevention measures

Table 4.15: Chi-square test results of Comparison of Behavioral Characteristics and Prevention Measures Between Control and Case Participants

	Control N (%)	Case N (%)	Total N (%)	p-value Fisher test
Using insecticide treated bed nets while sleeping				
Yes	411 (66.2)	39 (6.3)	450 (72.5)	< 0.001
No	3 (0.5)	168 (27.1)	171 (27.5)	
Ever sleeping outdoor in the last 2 years				
Yes	4.0 (0.6)	195 (31.4)	199 (32.0)	< 0.001
No	410 (66.0)	12 (1.9)	422 (68.0)	
Ever sleeping with windows opened in last 2 years				
Yes	4.0 (0.6)	192 (30.9)	196 (31.6)	< 0.001
No	410 (66.0)	15 (2.4)	425 (68.4)	
Had a habit of spending time outside home after sunset				
Yes	4.0 (0.6)	198 (31.9)	202 (32.5)	< 0.001
No	410 (66.0)	9 (1.4)	419 (67.5)	

The findings in Table (4.15) highlight significant behavioral differences between control and case participants in relation to leishmaniasis prevention. Control participants were significantly more likely to use insecticide-treated bed nets while sleeping, with 66.2% of controls doing so compared to only 6.3% of cases. Conversely, case participants exhibited behaviors that increased their risk of infection. These include a higher prevalence of sleeping outdoors (31.4%), sleeping with windows open (30.9%), and spending time outside the home after sunset (31.9%). All these associations were statistically significant (p-values less than 0.001). These findings suggest that using preventive measures such as bed nets and avoiding risky behaviors can significantly reduce the risk of leishmaniasis infection.

Overall, the data indicates that control participants are significantly more likely to use insecticide-treated bed nets, while case participants are significantly more likely to have behaviors such as sleeping outdoors, sleeping with windows open, and spending time outside after sunset. These behaviors were significantly linked to increased risk of leishmaniasis infection.

CHAPTER FIVE: RESULTS DISCUSSION, CONCLUSION AND RECOMMENDATIONS

This chapter will present discussion of the main findings of our study in relation to its objectives and research questions. Conclusion remarks and recommendations to community and decision makers will be presented. Also, Limitations of the current study will be presented.

5.1 Discussion of main findings

5.1.1. Distribution of Leishmaniasis by residence area:

The analysis underscores a distinct spatial distribution of leishmaniasis cases, with Yatta (32.9%) and A'rab ar Rashayida (27.5%) emerging as primary hotspots, followed by Bani Naem (13.0%). Peripheral areas such as Dura, Sa'ir, Za'tara, and Adh Dhahiriya contribute moderately between 3.4% and 4.8%, while Bethlehem and Hebron exhibit lower incidences at 1.4% and 2.4%, respectively. Meanwhile, Taffuh, Tarqumiya, Idhna, Halhul, Ar Rihiya, and Surif are minimally affected, each accounting for 1.0% or less of cases. These findings accentuate the necessity for targeted interventions in Yatta, A'rab ar Rashayida, and Bani Naem, with continued surveillance imperative in Bethlehem and Hebron to avert potential outbreaks. Notably, the concentration of cases in peripheral areas, as opposed to main cities, emphasizes the importance of geographically tailored approaches in disease control efforts.

The alignment of these findings with prior research conducted in Palestine enhances their reliability, highlighting the persistent challenge of leishmaniasis in rural areas. This is consistent with earlier research by Amro *et al.,* (2017), who identified coastal regions as having a heightened risk due to more favorable conditions for the vectors responsible for transmission. They emphasized the importance of considering socio-economic factors, such as migration, conflicts, urbanization, land use, and access to healthcare, in the design of control programs to prevent the emergence of new endemic areas. Recent studies by Ghatee *et al.,* (2023) support these trends by identifying key environmental factors—such as urban settings, orchards, agriculture, and minimum temperature—that significantly influence the occurrence of cutaneous leishmaniasis (CL).

The consistency of these findings across multiple studies, including those by Amane M. *et al.,* (2022), who found a significant association between socioeconomic factors and rural habitation (OR = 4.163; 95% CI: 2.91–5.96), underscores the broader relevance and applicability of these results in understanding and addressing the epidemiology of leishmaniasis. Furthermore, Alzahrani *et al.,* (2023) noted a significant association between residing in or around planted areas and the likelihood of CL occurrence (AOR 1.18, 95% CI 0.13-2.24; P<0.001). This is further supported by the observations of Jarallah *et al.,* (2022) and Okwor and Uzonna (2016), who highlighted that leishmaniasis primarily affects impoverished, remote rural communities with poor housing and limited access to modern healthcare facilities.

5.1. 2. Distribution of Leishmaniasis by affected body part:

Hands were the main affected body part, affecting 59.4% of patients, with a higher prevalence among males (43.4%) compared to females (15.9%). The legs are the second most common site, impacting 18.8% of patients, with 14.4% being males and 4.3% females. Infections on the neck occur in 9.7% of patients (5.7% males and 3.8% females), while the face accounts for 12.1% of cases (8.2% males and 3.8% females). This distribution indicates a higher prevalence of infection on the hands and legs, particularly among males. The overall data underscores the need for targeted protective measures for the most commonly affected body parts, particularly in males who exhibit higher infection rates in all categories.

These findings align with previous studies, such as those by Sbehat (2012), Reithinger *et al.,* (2005), Yanik et *al.,* (2004), Kassi *et al.,* (2008), and Vares *et al.,* (2013), which also identified the hands and legs as the most common infection sites for leishmaniasis. In current study the higher prevalence among males in all categories suggests occupational or behavioral factors that increase exposure to the sandfly vector. These consistent results across multiple studies underscore the importance of implementing targeted protective measures for the most affected body parts, particularly the hands and legs, and developing gender-specific strategies to reduce infection rates among males. Uthman MA, *et al.,* (2005) found that the lesions often develop on exposed body parts, such as the face and extremities. The mucous membranes of the mouth, nose, and throat cavities, as well as surrounding tissue, can be totally or partially destroyed by ulcerations that may result in lifetime scarring, which can cause severe psychological and/or social stigma, particularly among young girls

Another issue which is not searched by this study is the number of lesions among studied patients. The site and number of lesions(s) are an indication of the type of cutaneous (CL). *L. major* usually presents as multiple lesions (≥3) and *L.tropica* is more often on the nose **(**Klaus and Frankenburg, 1999; AL Jawabreh *et al*., 2004). According to Al-Jawabreh, A., *et al.,* (2017) cases caused by *L. tropica*, significantly, had a single lesion compared to cases caused by *L. major* (P = 0.0001), which, significantly, had multiple lesions (P = 0.0001). This and previous studies showed that CL is present in all Palestinian districts. Amro *et al.,* (217) found that around 77.3% of *L. tropica* CL and 57.7% of *L. major* CL caused single lesions which reflects that most of current study patients were CL patients.

This distribution indicates a higher prevalence of infection on the hands and legs, particularly among males. The overall finding highlights the need for targeted protective measures for the most commonly affected body parts, particularly in males who exhibit higher infection rates in all categories. Educational programs can play a vital role in this regard by promoting protective measures, particularly during activities like sleeping and gathering outdoors, where exposure is heightened. Emphasizing the use of covers for these vulnerable areas, especially at night, could significantly reduce the risk of cutaneous leishmaniasis. By raising awareness about these simple yet effective precautions, communities can be better equipped to protect themselves against this persistent threat.

5.1. 3. Distribution of Leishmaniasis by Source of infection:

The distribution of leishmaniasis cases in our study reveals a distinct pattern of transmission concentrated in peripheral and suburban areas, particularly those near borders and away from major urban centers. The majority of cases, accounting for 29.9%, were reported from the Zatara, A'rab ar Rashayida, and Al-dirat areas, underscoring these locations as significant hotspots for the disease. Other notable sources include Wadi Araba, Dimona, Beer Sheba, and Eilat, contributing 16.4% of the cases, and Massafer Bani Na'im with 14.5%. Jericho also emerged as a significant source, accounting for 9.6% of the cases.

These findings are consistent with previous research by Al-Jawabreh *et al.,* (2004), Amro *et al.,* (2009), and Sbehat (2012), who found that over 70% of cutaneous leishmaniasis (CL) patients were residents of suburban areas, although cases were reported from various geographical sites. This pattern, observed across different studies and time periods, highlights the persistent vulnerability of suburban and peripheral regions to leishmaniasis. The work of Azmi *et al.,* (2017) further supports this consistency, linking the re-emergence of leishmaniasis in these areas to environmental changes and human activities that may have reactivated previously existing genotypes.

The spread of leishmaniasis in our study is particularly notable in less populated and remote areas, such as near the Egypt border (2.8%) and North Palestine including Nablus (1.9%), with minimal yet notable cases from locations like Julan Israel and Dir Alsal near the 1967 border. These findings emphasize the complex dynamics of disease transmission in peripheral regions, where environmental shifts and human interventions are creating favorable conditions for the resurgence of the disease.

The alignment of our results with those from earlier studies reinforces the need for targeted public health interventions in these vulnerable areas. The consistency of findings across different geographical sites and time periods underscores the importance of monitoring suburban and peripheral regions closely. Effective control measures, tailored to the unique environmental and socio-economic conditions of these areas, are crucial in preventing the further spread of leishmaniasis and mitigating its impact on affected communities.

5.1.4. Distribution of participants by the type of house:

The findings proposed a significant disparity in housing types between leishmaniasis cases and controls. A higher proportion of cases (17.6%) reside in tents compared to 15.8% living in built houses. Conversely, among controls, 56.0% reside in built houses, with only 10.6% living in tents. This discrepancy suggests that living in tents may pose an elevated risk of contracting leishmaniasis. Housing conditions emerge as a critical factor in disease transmission, underscoring the potential impact of improved living conditions as a public health intervention to mitigate leishmaniasis incidence.

These results align with previous studies conducted locally, regionally, and internationally, which have identified housing characteristics as influential factors in leishmaniasis epidemiology. Mandal *et al.,* (2020) identified living in thatched houses and sleeping on the

ground floor as risk factors. Similarly, Ullah *et al.,* (2016) emphasized the role of household clustering, construction materials, and traditional practices. Maia *et al.,* (2016) found that staying in houses with sand backyards conferred possible protection against Leishmania infection. Additionally, Kiptui *et al.,* (2021) reported a significant association between staying in mud or cracked houses and leishmaniasis incidence. Sarmadi *et al.,* (2023) found that living in muddy houses, ruined buildings, or areas with stagnant water was related with likelihood of leishmaniasis.

Results show a distinct variation in housing types when comparison between the infected and the non-infected individuals. A higher proportion of infections were found among individuals staying in tents which hints that living in tent might be linked to an elevated susceptibility to be infected. These collective findings underscore the multifaceted nature of housing-related risk factors in leishmaniasis occurrence and transmission, emphasizing the importance of targeted interventions to address housing vulnerabilities and reduce disease burden.

5.1.5. Effect of socio-demographic factors on leishmaniasis transmission:

The analysis reveals significant findings regarding the socio-demographic characteristics of leishmaniasis cases and controls. Geographic variability is evident, with Hebron exhibiting a higher prevalence (22.2%) compared to Bethlehem (11.1%). Age is a notable factor, with elevated case proportions among individuals under 15 years (13.4%) and those aged 15-30 years (11.6%). Males constitute a larger proportion of the sample (68.9%), with a significant proportion being cases (24.0%), while females also show notable case percentages (30.1%). Education level, particularly basic school education, and occupation, such as farmers (9.5%) and students (11.8%), significantly influence leishmaniasis occurrence. Residency in villages is associated with a higher disease occurrence (29.8%) compared to camps (0.3%) and cities (3.2%). Income levels between 1880-4000 ILS are linked to higher case percentages (27.4%), and travel to endemic areas strongly correlates with leishmaniasis cases (9.5%). These findings underscore the critical role of socio-demographic factors in both disease transmission and prevention strategies.

These findings were in align with other studies. Wijerathna *et al.,* (2020) found that demographic factors associated with CL and the younger population was more affected group. Peter Lomurukai (2020), Sarmadi *et al.,* (2023), Terefe *et al.,* (2015) and Yared *et al.,* (2014) found that males reported higher case notification than females and the age groups were children and young adults. However, Alzahrani *et al.,* (2023) found that no significant associations were observed based on sex but on the other side highlighted that age, residence in planted areas, and occupation as key risk factors for leishmaniasis aligned with Sriwongpan *et al.,* (2021) who found infection risk factors included female gender, and increasing age. Bamorovat *et al.,* (2018) found that older age (≥51 years) which contradicted to our finding related to age as a risk factor.

Eid *et al.,* (2018) found that a 43% CL prevalence, with male sex identified as a key risk factor. Charoensakulchai *et al.,* (2020) found that risk factors for *L. martiniquensis* were female gender, recreational drug use, and comorbidities. Kiptui *et al.,* (2021) found that majority of the infected were uneducated (68%). Socio-demographic factors including education, income, residency characteristics were studied and reported to be risk factors for leishmaniasis infection (Yared *et*

al., 2014, Alzahrani *et al.,* 2023, Amane M. *et al.* 2022, Eid *et al.,* 2018, Bamorovat *et al.,* 2018, Maia *et al.,* 2016, Ullah *et al.,* 2016, Mandal *et al.,* 2020, and Wijerathna *et al.* 2020).

5.1.6. Effect of Environmental factors on leishmaniasis transmission:

The examination of environmental variables influencing CL transmission yields significant insights into potential disease risk factors. Table (4.6) elucidates the connection between outdoor environmental conditions and CL occurrence, revealing a robust association with factors such as decaying garbage, unclean (dirty) areas, wet soil, and proximity to water streams. These findings shown the crucial role of environmental cleanliness and sanitation in curtailing disease spread. Moreover, the spatial distribution of houses emerges as a crucial determinant, with peripheral locations exhibiting a higher incidence of the disease compared to central areas, as evidenced in Table (4.7).

Furthermore, housing conditions significantly impact disease transmission, with poor house conditions and higher household occupancy rates correlating with increased leishmaniasis cases, as delineated in Tables (4.8 and 4.9). Additional scrutiny in table 4.10 underscores the influence of factors like tent housing, overcrowding, inadequate sanitation, and the absence of window nets on disease transmission rates. R. Patil, R., & K. Chatterjee, P. (2024) found that poverty enhances the risk for Kala-azar. Poor housing and domestic sanitary conditions are good breeding ground for sandfly which is the vector for Visceral Leishmaniasis, as well as resting sites and their ease of sandfly contact with humans.

The analysis highlights that environmental factors such as decaying garbage, unclear areas, wet soil, and proximity to water streams show significant relationship with an increased risk of leishmaniasis, whereas gardening areas do not exhibit a significant correlation. This information is crucial for public health interventions aimed at reducing the incidence of leishmaniasis by targeting environmental improvements. Analysis indicates that higher number of family members occupying house or bedroom is significantly associated with increased transmission of leishmaniasis. This could indicate the impact of household occupancy rate in the spread of the disease, highlighting the need for interventions aimed at improving living conditions.

These results underline the necessity for targeted involvements aimed at enhancing housing conditions and environmental sanitation to mitigate leishmaniasis risk in affected communities. Moreover, these results align with previous research, highlighting the pivotal role of environmental factors in leishmaniasis epidemiology (Amane M. *et al.,* 2022; Valero & Uriarte, 2020; Alzahrani *et al.,* 2023; Yared *et al.,* 2014; Sarmadi *et al.,* 2023; Terefe *et al.,* 2015; Kiptui *et al.,* 2021; Bamorovat and colleagues., 2018; Ullah *et al.,* 2016; Mandal *et al.,* 2020).

Additionally, Yupari-Azabache *et al.,* (2023) found that households with basic access to infrastructure were similarly vulnerable, reinforcing the need for a comprehensive approach to address the socio-environmental determinants of the disease. Jarallah HM. *et al.,* (2022) found that VL has a dynamic epidemiology factors can change under the influence of climate, ecology, behavior of humans, vectors and reservoirs.

5.1.7. Effect of having animals on leishmaniasis transmission:

The analysis of animals' impact on leishmaniasis transmission reveals significant associations between certain animals and disease incidence. Households with animals, particularly dogs, cats, chickens, and rodents, show a notably higher prevalence of leishmaniasis cases compared to those without animals. Specifically, existence of dogs and cats significantly elevates the risk of leishmaniasis, with odds ratios of 2.6 and 2.1, respectively. Furthermore, chickens and rodents pose a substantial risk, with odds ratios of 3.8 and 13.2, respectively. In contrast, larger livestock like cattle, sheep, goats, and cows do not exhibit a significant association with leishmaniasis transmission. However, the presence of rocky hyraxes and foxes, though less common, also shows a noteworthy association with leishmaniasis cases. These findings underscore the importance of targeted interventions to control animal populations, particularly dogs, cats, chickens, rodents, rocky hyraxes, and foxes, to mitigate leishmaniasis transmission. Additionally, Figure 5.4 highlights a higher prevalence of rodents, rats, rocky hyraxes, and foxes in leishmaniasis cases, indicating a potential link between these animals and disease transmission and offering valuable insights for vector control and disease prevention strategies. Rock hyraxes are were incriminated as the reservoir hosts of *L. tropica*, a parasitic microorganism that causes the disease leishmaniasis in humans and other mammals (Svobodová *et al.,* 2006).

Similar results were observed in previous studies. Lehlewa AM, *et al.,* (2021) found that CL cases were more likely than controls to report a history of having rodents inside the house (OR 5.15, 95% CI 3.56-7.47), having chickens, sheep, or both (OR 3.44, 95% CI 2.48-4.75), having a mixture of dogs and sheep or of dogs and chickens within a distance of less than 100 meters (OR 3.92, 95% CI 2.59-5.94). Sbehat, (2012), reported rats and dogs around patients' houses, aligning with our findings. Ullah *et al.,* (2016), suggested that keeping cattle indoors at night could pose a risk. Sriwongpan *et al.,* (2021), recorded the existence of animal enclosures in housing areas as a risk factor for leishmaniasis infection. Yared *et al.,* (2014), associated goat ownership with elevated odds of VL (OR = 6.4). Amane M. *et al.,* (2022) also linked the presence of animals with socioeconomic and environmental factors associated with cutaneous leishmaniasis (CL). Additionally, Olga Vinitsky *et al.,* (2010) found that infected individuals were existed in marginal line of two neighborhoods, close to the habitats of the rock hyraxes, further supporting our findings.

5.1.8. Topography and Climate risk factors:

The analysis of leishmaniasis cases and controls concerning residence area topography and climate risk factors reveals significant associations, providing insights for public health strategies. Living near natural environments such as caves, crevices, and stone fences is linked to a notably higher risk of leishmaniasis, indicating these areas as potential habitats for disease vectors. Conversely, urban areas exhibit lower risk due to fewer vector habitats and better living conditions. Agricultural areas show a moderate presence of cases, suggesting a level of risk related to farming activities and vector exposure. Regarding climate factors, areas with below-average rainfall have a significantly higher proportion of cases, indicating that drier conditions

might favor vector activity and disease transmission. Conversely, areas with above-average rainfall show minimal cases, suggesting less favorable conditions for vector proliferation.

Regarding rainfall in Palestine from 2014 to 2023, the association between annual rainfall and leishmaniasis incidence in Hebron and Bethlehem districts over the examined period showed no statistically significant correlation. Cutaneous leishmaniasis cases varied annually, with peaks in certain years, while visceral leishmaniasis cases remained consistently low. Similarly, rainfall fluctuated over the years (seasonal variation) in both districts, yet no significant correlation with leishmaniasis incidence was observed. Overall, the data suggests that other factors beyond rainfall might play a more significant role in leishmaniasis spreads in these regions during the examined period. Amro *et al.,* (2017) found that seasonal occurrence of CL cases showed that most cases (74.2%) admitted to the hospital between November and March, *L. major* cases from November till January (69.4%), and *L. tropica* cases mainly in January and February (41%). In contradict Valero & Uriarte, (2020) found the possible effect of climatic change including rainfall on the incidence of leishmaniasis. Nili *et al.,* (2021) showed a seasonal pattern, peaking from August to October. Meteorological variables like temperature, humidity, rainfall, and sunshine hours were associated with CL incidence. Ghatee *et al.,* (2023) identified urban settings, orchards, agriculture, and minimum temperature as significant determinants of CL occurrence in the region. Yupari-Azabache *et al.,* 2023 identified direct associations between annual rainfall, humid forest areas, and mortality from transmissible diseases with leishmaniasis cases.

The examination of leishmaniasis cases and controls concerning residence area topography and climate risk factors yields significant associations, offering valuable insights for public health strategies. Proximity to natural environments like caves, crevices, and stone fences is strongly correlated with a heightened risk of leishmaniasis, indicating these areas as potential breeding grounds for disease vectors. Concerning climate factors, regions experiencing below-average rainfall exhibit a notably higher proportion of cases, implying that drier conditions may facilitate vector activity and disease transmission. Conversely, areas with above-average rainfall show minimal cases, indicating less conducive conditions for vector proliferation. Temperature analysis reveals associations between leishmaniasis cases and both minimum and medium temperatures, emphasizing temperature as a significant risk factor. These findings assure the magnitude of taking environmental and climatic factors into consideration while planning suited interventions and strategies for leishmaniasis prevention and control.

Our data on rainfall and temperature fluctuation (annual or seasonal variation) could be not enough to illustrate the association between CL occurrence and rainfall and temperature, and this lead to conduct future deeper research on this issue.

5.1.9. Behavioral characteristics and prevention measures:

The outcomes delineated in Table 4.15 underscore notable disparities in behavioral patterns between control and case cohorts concerning leishmaniasis prevention strategies. Control participants exhibit a markedly higher propensity to utilize insecticide-treated bed nets during sleep, with 66.2% adhering to this practice compared to a mere 6.3% among cases. Conversely,

case participants demonstrate behaviors conducive to heightened infection risk, including a greater prevalence of outdoor sleeping (31.4% cases vs. 0.6% controls).

Findings are in consistence with others came by different studies. Kiptui *et al.,* (2021) similarly noted associations between visceral leishmaniasis and outdoor sleeping or proximity to acacia trees and ant hills near residences ($p<0.01$). Additionally, case participants exhibit a higher incidence of sleeping with windows ajar (30.9% cases vs. 0.6% controls) and engaging in outdoor activities post-sunset (31.9% cases vs. 0.6% controls), all statistically significant with p-values below 0.001. These findings accentuate the efficacy of preventive measures like bed net usage and the detrimental impact of risky behaviors on leishmaniasis vulnerability. However, it's noteworthy that while Maia *et al.,* (2016) did not find significant protective effects with repellents and bed nets, our findings align with Yared *et al.,* (2014), indicating elevated visceral leishmaniasis odds associated with prolonged field exposure (OR = 1.1), conversely lower odds linked to indoor sleeping (OR = 0.2) and outdoor sleeping under bed nets (OR = 0.1). Conversely, Alzahrani *et al.,* (2023) observed no significant associations based on gender (AOR 1.4, 95% CI 0.7–1.6; P=0.11), educational attainment (P=0.072), or preventive measure utilization (P>0.05). Overall, the data underscores the heightened propensity of control participants to employ insecticide-treated bed nets compared to cases, while the latter group exhibits behaviors significantly associated with augmented leishmaniasis infection risk. Lehlewa AM, *et al.,* (2021) also found that cases were more likely than controls to report a history of bed net use (OR 1.72, 95% CI 1.08-2.72), and sleeping outside or a mixture of inside and outside (OR 4.01, 95% CI 1.32-12.19).

Overall, the data indicates that control participants are significantly more likely to use insecticide-treated bed nets, while case participants are significantly more likely to have behaviors such as sleeping outdoors, sleeping with windows open, and spending time outside after sunset. Risk of getting leishmaniasis infection found to be associated with participants' behaviors.

5.2 Conclusion

In conclusion, our case-control study sheds light on the complex interplay between social and environmental determinants of leishmaniasis in the Hebron and Bethlehem districts of the West Bank, Palestine.

The findings from our study provide a comprehensive analysis of the distribution, risk factors, and epidemiological patterns of leishmaniasis in the studied regions. The distinct spatial distribution, particularly in peripheral and rural areas like Yatta and A'rab ar Rashayida, highlights the need for geographically focused public health interventions. The significant association between environmental factors such as decaying garbage, wet soil, and proximity to water streams with the incidence of leishmaniasis underscores the critical role of environmental management in disease control.

The study also reveals a marked disparity in disease prevalence based on socio-demographic factors, with higher incidence among males, younger age groups, and individuals living in tents or poorly constructed houses. These findings align with previous research, emphasizing the vulnerability of certain populations due to occupational exposure, housing conditions, and socio-economic factors.

Moreover, the analysis of the body parts affected by leishmaniasis, particularly the hands and legs, points to the necessity of targeted protective measures, especially among males who are disproportionately affected. The study also identifies a strong correlation between the presence of animals, particularly dogs, cats, chickens, and rodents, and the transmission of leishmaniasis, indicating the need for animal control measures as part of an integrated disease management strategy.

In conclusion, this study highlights the multifaceted nature of leishmaniasis transmission, driven by a combination of environmental, socio-demographic, and animal-related factors. The consistency of these findings with prior research underscores the reliability of the results and reinforces the need for targeted, context-specific interventions. By addressing the unique environmental and socio-economic conditions of the affected regions, public health authorities can effectively mitigate the spread of leishmaniasis and reduce its impact on vulnerable communities. The study calls for ongoing surveillance, community education, and the implementation of tailored public health strategies to prevent further outbreaks and protect at-risk populations.

5.3 Recommendations

Recommendations for patients:

1. Utilize Protective Measures: Patients should prioritize the use of insecticide-treated bed nets during sleep to minimize the risk of contracting leishmaniasis, especially in areas with known transmission.
2. Avoid Risky Behaviors: Patients should avoid sleeping outdoors, keeping windows open during the night, and spending time outside after sunset, as these behaviors significantly increase the risk of infection.
3. Seek Prompt Medical Attention: Individuals experiencing symptoms suggestive of leishmaniasis, such as skin lesions, fever, and fatigue, should seek prompt medical evaluation and treatment to prevent complications and further transmission.

Recommendations for Decision Makers (Ministry of Health and Local Government):

1. Enhance Surveillance and Control Measures: Authorities should prioritize enhanced surveillance efforts in hotspot areas identified by our study, such as Yatta, Alrashaydah, and Bani Naem, to monitor disease trends and implement targeted control measures.
2. Improve Housing Conditions: Investing in housing infrastructure, particularly in peripheral regions near borders, can help reduce disease transmission by improving living conditions and reducing vector breeding sites.

3. Promote Public Awareness: Implementing public awareness campaigns to educate communities about leishmaniasis transmission, preventive measures, and early detection can empower individuals to protect themselves and seek timely medical care.

For Researchers:

1. Further Investigate Environmental Determinants: Future research should delve deeper into the environmental factors influencing leishmaniasis transmission, such as the role of specific habitats, climate variability, and urbanization, to enhance understanding and inform targeted interventions.
2. Explore Socioeconomic Drivers: Investigating the socioeconomic determinants of leishmaniasis, including income levels, education, and occupation, can provide valuable insights into vulnerability factors and guide equitable intervention strategies.
3. Evaluate Intervention Effectiveness: Conducting longitudinal studies to assess the effectiveness of interventions targeting housing improvements, vector control measures, and public health campaigns can inform evidence-based policy decisions and enhance disease control efforts.

5.4 Limitations and strengths of the Study

5.4.1. Limitations:

Methodological and Data Limitations:

1. Data Quality: Incomplete records and retrospective data collection may affect the accuracy and reliability of our findings. Recall Bias: As with many case-control studies, recall bias may be present. Participants might not accurately remember or report their exposure to risk factors, such as specific environmental conditions or their behaviors.
2. Selection Bias: Due to difficulty in obtaining the names and addresses of registered cases in both Districts. The selection of cases and controls was based on simple and easy to reach (i.e., selecting cases and controls were not systematically) which might introduce bias if they are not representative of the broader population.
3. Confounding Variables: There may be confounding factors that were not measured or controlled for, which could influence the observed associations between risk factors and leishmaniasis. For instance, other socio-economic or environmental factors not included in the study could play a role.
4. Environmental and Behavioral Variables: Measuring environmental and behavioral variables accurately can be challenging. Factors like proximity to animal hosts or specific agricultural practices might not be captured in detail, potentially affecting the analysis.
5. Biological Variation: Differences in Leishmania parasites, vector species, and human host factors (not studied) may limit the applicability of our results to other settings.
6. Generalizability: Findings are specific to Hebron and Bethlehem districts and may not apply to other regions or different time periods.

External Limitations

1. Socio-Political Factors: Political instability or social disruptions in the study areas could impact the accuracy of data collection and the generalizability of the findings.
2. Resource and Time Constraints: Limited funding, staffing, and time may have restricted the scope and depth of our data collection and analysis.
3. Incomplete or not enough information related to registered cases, which hindered us to reach all areas in which they were missed cases.

5.4.2. Strengths:

1. **Comprehensive Risk Factor Analysis**: The study provides a detailed examination of multiple risk factors, including animal ownership, topography, and climate, offering a holistic understanding of the elements influencing leishmaniasis occurrence. This comprehensive approach allows for a more nuanced understanding of the disease's spread.
2. **Large Sample Size**: With 621 cases analyzed, the study benefits from a robust sample size, which reduces the margin of error and increases the study's statistical power.
3. **Geographic Coverage**: The study includes data from various regions, including urban, agricultural, and natural environments, ensuring that the findings are relevant to a wide range of settings. This diversity strengthens the study's applicability to different geographic contexts.
4. **Use of different Statistical Methods**: The application of chi-square tests, odds ratios, and confidence intervals ensures rigorous analysis, providing strong evidence for the associations identified between risk factors and leishmaniasis occurrence.
5. **Focus on Environmental Factors**: By examining the role of topography and climate, the study addresses critical yet often overlooked aspects of leishmaniasis transmission. This focus on environmental determinants is essential for developing effective prevention and control strategies.
6. **Relevance to Public Health**: The study's findings have direct implications for public health, particularly in regions where leishmaniasis is endemic. The identification of high-risk areas and populations can guide resource allocation and policy-making to combat the disease more effectively.

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Appendices

Appendix 1: Case Research Questionnaire

Research Questionnaire
استبانة بحث

Environmental and Social Determinants and Risk Factors for Cutaneous Leishmaniasis: A Case- Control Study in Hebron and Bethlehem Governorates
"المحددات البيئة والاجتماعية وعوامل الخطر لمرض الليشمانيا في فلسطين: دراسة مقارنة في محافظتي الخليل وبيت لحم".

المواطن/ة الكريم/ة

بعد التحية:

انا طالبة دراسات عليا في برنامج مكافحة العدوى في جامعة القدس. لقد تم اختيارك لمشاركتي في دراستي البحثية بعنوان: "**المحددات البيئة والاجتماعية وعوامل الخطر لمرض الليشمانيا في فلسطين: دراسة مقارنة في محافظتي الخليل وبيت لحم**"، حيث ان الهدف منها هو التعرف على المحددات البيئة والاجتماعية وعوامل الخطر لمرض الليشمانيا في فلسطين: دراسة مقارنة في محافظتي الخليل وبيت لحم وتم اختيار الموضوع لوجود نقص في الابحاث حول هذا الموضوع. المشاركة تطوعية فإذا اخترت المشاركة في الدراسة، فسوف يستغرق الأمر من 20 إلى 35 دقيقة تقريبًا من وقتك وسيتم اخفاء هوية المشارك في هذه الدراسة. لكم الحرية في عدم المشاركة أو الانسحاب من الدراسة. إذا رغبت في الانسحاب يمكنك ذلك في أي وقت تريده، أي معلومات مقدمة من قبلك سيتم إلغائها وستبقى جميع اجاباتك في غاية السرية. فقط أولئك الذين يشاركون بشكل مباشر في هذا المشروع سيكون لهم حق الوصول إلى البيانات. سوف تتخذ جميع الخطوات لحماية هويتك. لا توجد مخاطر متوقعة في هذه الدراسة. إذا كان لديك أية أسئلة حول الدراسة، يرجى التواصل معي عبر الايميل.

مرام مخارزة: makharzehmaram@gmail.com **المشرف: دكتور ياسر عيسى**

شكرًا لك على الوقت الذي قضيته في مساعدتي في هذا البحث.

Part 1: The main questionnaire

Part One: Socio-demographic factors		الجزء الأول: العوامل الاجتماعية والديموغرافية
1.	**Age in years**	**العمر بالسنوات**
	< 15 years	□ اقل من 15 سنة
	15-30 years	□ من 15-30سنة
	31-45 years	□ من 31-45 سنة
	46-60years	□ من 46-60 سنة
	>60 years	□ اكثر من 60 سنة
2.	**Gender**	**النوع الاجتماعي (الجنس)**
	Male	□ ذكر
	Female	□ انثى
3.	**Marital Status**	**الحالة الاجتماعية**
	Married	□ متزوج / ة
	Single	□ اعزب / عزباء
	Divorced	□ مطلق/ة
	Widow	□ ارمل/ة
4.	**Education**	**المؤهل العلمي**
	Basic school	□ المرحلة الاساسية (المدرسة)
	University and college	□ المرحلة الجامعية
	Higher education	□ التعليم العالي
5.	**Main Occupation**	**الوظيفة الرئيسة**
	Farmer	□ مزارع
	Government server	□ موظف حكومي مدني
	Laborer	□ عامل
	Private sector employee	□ موظف قطاع خاص
	Self-employee	□ اعمال حرة
	Household	□ رب/ة اسرة
	Student	□ طالب/ة
6.	**Residency**	**مكان الاقامة**
	Camp	□ مخيم
	Village	□ قرية
	City	□ مدينة
7.	**Monthly income (In sheikel)**	**الدخل الشهري**
	< 1880 ILS	□ اقل من 1880 شيقل
	1880-4000 ILS	□ من 1880-4000 شيقل

	4001-6000 ILS	□ من 4001-6000 شيقل
8.	**Travel to endemic area**	**السفر الى مناطق موبوءة بالمرض**
	Yes	□ نعم
	No	□ لا
Part Two: Environmental factors and indoor characteristics		**الجزء الثاني: العوامل البيئية والخصائص الداخلية**
9.	**Decaying Garbage**	**القمامة المتحللة**
	Present	□ موجود
	Absent	□ غير موجود
10.	**House condition**	**ظروف المنزل**
	Poor	□ سيء (متدني)
	Moderate	□ مقبول (متوسط)
	Good	□ جيد (حسن)
12.	**Unclear areas**	**منطقة غير نظيفة**
	Present	□ موجود
	Absent	□ غير موجود
13.	**Areas with wet soil**	**منطقة فيها تربة رطبة او مبللة**
	Present	□ موجود
	Absent	□ غير موجود
14	**Gardening areas**	**مناطق البستنة او الحدائق**
	Present	□ موجود
	Absent	□ غير موجود
15.	**Water Streams**	**جداول مياه**
	Present	□ موجود
	Absent	□ غير موجود
16.	**Animals owned or frequently visiting the home / near or around house**	**الحيوانات التي تمتلكها أو موجودة بالقرب من المنزل أو حوله**
	Dogs	□ كلاب
	Cats	□ قطط
	Cattle, sheep, goats, cows	□ الماشية والأغنام والماعز والأبقار
	Chicken	□ دجاج
	Rodents and rats	□ قوارض وجرذان
	Hens	□ حمام
	Rocky hyrax	□ وبر صخري
	Foxes	□ الثعالب
17.	**Location of the house**	**موقع المنزل**
	Center of the domestic area	□ وسط البلد
	Peripheral of the domestic area	□ على اطراف البلد

18.	**Persons per house**	**عدد افراد الاسرة في المنزل**
	1-5	□ من 1-5 افراد
	>5	□ اكثر من 5 افراد
19.	**Persons per bedroom**	**عدد الافراد لكل غرفة نوم**
	one or two	□ واحد او اثنان
	three or more	□ ثلاثة واكثر
20.	**Type of wall covering**	**نوع تغطية الجدران**
	Unplaster/ normal paint	□ طلاء غير لاصق / عادي
	Plastered / oily paint	□ جص / دهان زيتي
	Mixed	□ مختلط
21.	**Type of housing**	**نوع وهيكلة المنزل**
	Underground	□ ارضي تحت ارضي
	One floor	□ طابق واحد
	Multi-floors	□ طوابق متعددة
22.	**Staying Place**	**مكان المكوث**
	In first floor	□ في الطابق الاول
	In upper floor	□ في الطوابق العلوية
23.	**Living in a house with cracked wall**	**العيش في منزل به جدار متصدع**
	Yes	□ نعم
	No	□ لا
24.	**Living in a house with cracked floors**	**العيش في منزل به ارضيات متصدعة**
	Yes	□ نعم
	No	□ لا
25.	**Window of the house**	**نوافذ المنزل**
	With net	□ مع منخل (شبك)
	Without net	□ بدون منخل (شبك)
26.	**Materials in the yards**	**المواد في الساحات**
	Stones	□ حجارة
	leaves, and tree trunk	□ اوراق وجذع اشجار
27.	**Presence of construction waste and the deposition of garbage near the house** **وجود مخلفات البناء القمامة بالقرب من المنزل**	
	Yes	□ نعم
	No	□ لا
28.	**Presence of crop farms in the vicinity**	**وجود مزارع المحاصيل في المنطقة المجاورة**
	Yes	□ نعم
	No	□ لا
29.	**Presence of a nearby forest or thicket in the vicinity**	**وجود غابة أو غابة قريبة في المنطقة المجاورة**
	Yes	□ نعم

	No	□ لا
30.	**Sanitation**	**الصرف الصحي**
	Inadequate access to sanitation	□ عدم كفاية الوصول إلى الصرف الصحي
	Adequate access to sanitation	□ الوصول الملائم إلى الصرف الصحي
31.	**Sewage system/waste management**	**نظام الصرف الصحي / إدارة النفايات**
	Present	□ موجود
	Absent	□ غير موجود
32.	**Natural environment**	**البيئة الطبيعية**
	Caves	□ كهوف
	Crevices	□ شقوق
	Stone fences	□ اسوار حجرية
	Agricultural area	□ منطقة زراعية
33.	**Rainfall**	**الامطار**
	<the annual average	□ اقل من المعدل السنوي
	=the annual average	□ مساو للمعدل السنوي
	>the annual average	□ اكثر من المعدل السنوي
34.	**Temperature**	**درجات الحرارة**
	Average monthly minimum temperature	□ متوسط درجة الحرارة الصغرى الشهرية
	Average monthly maximum temperature	□ متوسط درجة الحرارة القصوى الشهرية
	Average monthly medium temperature	□ المتوسط الشهري لدرجة الحرارة المتوسطة
Part Three: Knowledge about Leishmaniasis		**المعرفة بمرض الليشمانيا**
35.	**Heard about disease (before infection)**	**سمعت عن المرض (قبل الاصابة)**
	Yes	□ نعم
	No	□ لا
36.	**Source of information about disease**	**مصدر المعلومات عن المرض**
	TV/Radio	□ التلفاز / الاذاعة
	Printed media	□ وسائط مطبوعة
	Friend	□ صديق
	Health worker	□ عامل صحي
37.	**Family knowledge of the vector**	**معرفة الأسرة بالناقل للمرض**
	Yes	□ نعم
	No	□ لا
Part Four: Behavioral characteristics and prevention measures الجزء الرابع: الخصائص السلوكية وتدابير الوقاية		
38.	**Use insecticide-treated bed nets while sleeping**	**استخدم الناموسيات المعالجة بالمبيدات أثناء النوم**
	Yes	□ نعم
	No	□ لا

39.	**Ever sleeping outdoors in the last 2 years**	**من أي وقت مضى النوم في الهواء الطلق في العامين الماضيين**
	Yes	□ نعم
	No	□ لا
40.	**Ever sleeping with windows open in the last 2 years**	**من أي وقت مضى في النوم مع فتح النوافذ في العامين الماضيين**
	Yes	□ نعم
	No	□ لا
41.	**Had a habit of spending time outside the home after sunset**	**اعتاد قضاء الوقت خارج المنزل بعد غروب الشمس**
	Yes	□ نعم
	No	□ لا

Thank you

Appendix2: Control's research questionnaire

Research Questionnaire

Environmental and Social Determinants and Risk Factors for Cutaneous Leishmaniasis: A Case- Control Study in Hebron and Bethlehem Governorates

المواطن/ة الكريم/ة

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مرام مخارزة: makharzehmaram@gmail.com **المشرف: دكتور ياسر عيسى**

شكرًا لك على الوقت الذي قضيته في مساعدتي في هذا البحث

1.	**District** **المحافظة**	
	Hebron	**الخليل**
	Bethlehem	**بيت لحم**
Part One: Socio-demographic factors		**الجزء الأول: العوامل الاجتماعية والديموغرافية**
1.	**Age in years**	**العمر بالسنوات**
	< 15 years	اقل من 15 سنة
	15-30 years	من 15-30سنة
	31-45 years	من 31-45 سنة
	46-60years	من 46-60 سنة
	>60 years	اكثر من 60 سنة
2.	**Gender**	**النوع الاجتماعي (الجنس)**
	Male	ذكر
	Female	انثى
3.	**Marital Status**	**الحالة الاجتماعية**
	Married	متزوج / ة
	Single	اعزب / عزباء
	Divorced	مطلق/ة
	Widow	ارمل/ة
4.	**Education**	**المؤهل العلمي**
	Basic school	المرحلة الاساسية (المدرسة)
	University and college	المرحلة الجامعية
	Higher education	التعليم العالي
5.	**Main Occupation**	**الوظيفة الرئيسة**
	Farmer	مزارع
	Government server	موظف حكومي مدني
	Laborer	عامل
	Private sector employee	موظف قطاع خاص
	Self-employee	اعمال حرة
	Household	رب/ة اسرة
	Student	طالب/ة
6.	**Residency**	**مكان الاقامة**
	Camp	مخيم
	Village	قرية
	City	مدينة
7.	**Monthly income (In sheikel)**	**الدخل الشهري**
	< 1880 ILS	اقل من 1880 شيقل

	1880-4000 ILS	□ من 1880-4000 شيقل
	4001-6000 ILS	□ من 4001-6000 شيقل
8.	**Travel to endemic area**	**السفر الى مناطق موبوءة بالمرض**
	Yes	□ نعم
	No	□ لا
Part Two: Environmental factors and indoor characteristics		**الجزء الثاني: العوامل البيئية والخصائص الداخلية**
9.	**Decaying Garbage**	**القمامة المتحللة**
	Present	□ موجود
	Absent	□ غير موجود
10.	**House condition**	**ظروف المنزل**
	Poor	□ سيء (متدني)
	Moderate	□ مقبول (متوسط)
	Good	□ جيد (حسن)
12.	**Unclear areas**	**منطقة غير نظيفة**
	Present	□ موجود
	Absent	□ غير موجود
13.	**Areas with wet soil**	**منطقة فيها تربة رطبة او مبللة**
	Present	□ موجود
	Absent	□ غير موجود
14	**Gardening areas**	**مناطق البستنة او الحدائق**
	Present	□ موجود
	Absent	□ غير موجود
15.	**Water Streams**	**جداول مياه**
	Present	□ موجود
	Absent	□ غير موجود
16.	**Animals owned or frequently visiting the home / near or around house**	**الحيوانات التي تمتلكها أو موجودة بالقرب من المنزل أو حوله**
	Dogs	□ كلاب
	Cats	□ قطط
	Cattle, sheep, goats, cows	□ الماشية والأغنام والماعز والأبقار
	Chicken	□ دجاج
	Rodents and rats	□ قوارض وجرذان
	Hens	□ حمام
	Rocky hyrax	□ وبر صخري
	Foxes	□ الثعالب
17.	**Location of the house**	**موقع المنزل**
	Center of the domestic area	□ وسط البلد

	Peripheral of the domestic area	□ على اطراف البلد
18.	**Persons per house**	**عدد افراد الاسرة في المنزل**
	1-5	□ من 1-5 افراد
	>5	□ اكثر من 5 افراد
19.	**Persons per bedroom**	**عدد الافراد لكل غرفة نوم**
	one or two	□ واحد او اثنان
	three or more	□ ثلاثة واكثر
20.	**Type of wall covering**	**نوع تغطية الجدران**
	Unplaster/ normal paint	□ طلاء غير لاصق / عادي
	Plastered / oily paint	□ جص / دهان زيتي
	Mixed	□ مختلط
21.	**Type of housing**	**نوع وهيكلة المنزل**
	Underground	□ ارضي تحت ارضي
	One floor	□ طابق واحد
	Multi-floors	□ طوابق متعددة
22.	**Staying Place**	**مكان المكوث**
	In first floor	□ في الطابق الاول
	In upper floor	□ في الطوابق العلوية
23.	**Living in a house with cracked wall**	**العيش في منزل به جدار متصدع**
	Yes	□ نعم
	No	□ لا
24.	**Living in a house with cracked floors**	**العيش في منزل به ارضيات متصدعة**
	Yes	□ نعم
	No	□ لا
25.	**Window of the house**	**نوافذ المنزل**
	With net	□ مع منخل (شبك)
	Without net	□ بدون منخل (شبك)
26.	**Materials in the yards**	**المواد في الساحات**
	Stones	□ حجارة
	leaves, and tree trunk	□ اوراق وجذع اشجار
27.	**Presence of construction waste and the deposition of garbage near the house**	**وجود مخلفات البناء القمامة بالقرب من المنزل**
	Yes	□ نعم
	No	□ لا
28.	**Presence of crop farms in the vicinity**	**وجود مزارع المحاصيل في المنطقة المجاورة**
	Yes	□ نعم
	No	□ لا
29.	**Presence of a nearby forest or thicket in the vicinity**	**وجود غابة أو غابة قريبة في المنطقة المجاورة**

	Yes	□ نعم
	No	□ لا
30.	**Sanitation**	**الصرف الصحي**
	Inadequate access to sanitation	□ عدم كفاية الوصول إلى الصرف الصحي
	Adequate access to sanitation	□ الوصول الملائم إلى الصرف الصحي
31.	**Sewage system/waste management**	**نظام الصرف الصحي / إدارة النفايات**
	Present	□ موجود
	Absent	□ غير موجود
32.	**Natural environment**	**البيئة الطبيعية**
	Caves	□ كهوف
	Crevices	□ شقوق
	Stone fences	□ اسوار حجرية
	Agricultural area	□ منطقة زراعية
33.	**Rainfall**	**الامطار**
	<the annual average	□ اقل من المعدل السنوي
	=the annual average	□ مساو للمعدل السنوي
	>the annual average	□ اكثر من المعدل السنوي
34.	**Temperature**	**درجات الحرارة**
	Average monthly minimum temperature	□ متوسط درجة الحرارة الصغرى الشهرية
	Average monthly maximum temperature	□ متوسط درجة الحرارة القصوى الشهرية
	Average monthly medium temperature	□ المتوسط الشهري لدرجة الحرارة المتوسطة
Part Three: Knowledge about Leishmaniasis		**المعرفة بمرض الليشمانيا**
35.	**Heard about disease (before infection)**	**سمعت عن المرض (قبل الاصابة)**
	Yes	□ نعم
	No	□ لا
36.	**Source of information about disease**	**مصدر المعلومات عن المرض**
	TV/Radio	□ التلفاز / الاذاعة
	Printed media	□ وسائط مطبوعة
	Friend	□ صديق
	Health worker	□ عامل صحي
37.	**Family knowledge of the vector**	**معرفة الأسرة بالناقل للمرض**
	Yes	□ نعم
	No	□ لا
Part Four: Behavioral characteristics and prevention measures الجزء الرابع: الخصائص السلوكية وتدابير الوقاية		
38.	**Use insecticide-treated bed nets while sleeping**	**استخدم الناموسيات المعالجة بالمبيدات أثناء النوم**
	Yes	□ نعم

	No	لا
39.	**Ever sleeping outdoors in the last 2 years**	**من أي وقت مضى النوم في الهواء الطلق في العامين الماضيين**
	Yes	نعم
	No	لا
40.	**Ever sleeping with windows open in the last 2 years**	**من أي وقت مضى في النوم مع فتح النوافذ في العامين الماضيين**
	Yes	نعم
	No	لا
41.	**Had a habit of spending time outside the home after sunset**	**اعتاد قضاء الوقت خارج المنزل بعد غروب الشمس**
	Yes	نعم
	No	لا

Thank you

Appendix 3: Permission of MOH

State of Palestine
Ministry of Health
Education in Health and Scientific
Research Unit

دوله فلسطين
وزارة الصحة
وحدة التعليم الصحي
والبحث العلمي

Ref.: .....
Date:.....

الرقم: ع ص/ ٥٥٩/ ٢٠١٩
التاريخ: ٢٠١٩/٠٥/٢٣

عطوفة الوكيل المساعد لشؤون الصحة العامة وصحة الاسرة المحترم،،،

تحية واحترام،،،

الموضـــوع: تسهيل مهمة بحث

يرجى تسهيل مهمة الطالبة: مرام مخارزة، برنامج ماجستير الوقاية وضبط الامراض المعدية– جامعة القدس، لعمل بحث بعنوان:

'Environmental and social determinants and risk factors for Leishmaniasis in Palestine: case control study in Hebron and Bethlehem Districts'

حيث ستقوم الطالبة بجمع معلومات من خلال تعبئة استبانة من قبل افراد اسرة مخالطين (بعد اخذ موافقتهم)، وذلك في:

- مديريات الصحة في محافظات : بيت لحم والخليل

مع العلم أن مشرف الدراسة: د. ياسر عيسى.

على ان يتم الالتزام بالمحافظة على اخلاقيات البحث العلمي وسرية المعلومات، وعدم التعرض للمعلومات التعريفية للمشاركات في البحث.
على ان يتم تزويد الوزارة بنسخة PDF من نتائج البحث، التعهد بعدم النشر لحين الحصول على موافقة وزارة الصحة.

د. عبد الله القواسمي
رئيس وحدة التعليم الصحي والبحث العلمي

نسخة: عميد كلية الصحة العامة المحترم/ جامعة القدس

Telfax.:09-2333901 scientificresearch.dep@gmail.com تلفاكس: 09-2333901

Appendix 4: Consent Form

موافقة على المشاركة في بحث علمي.

عنوان البحث:

" المحددات البيئة والاجتماعية وعوامل الخطر لمرض الليشمانيا في فلسطين: دراسة مقارنة في محافظتي الخليل وبيت لحم ".

Environmental and Social Determinants and Risk Factors for Cutaneous Leishmaniasis: A Case- Control Study in Hebron and Bethlehem Governorates

اسم الباحث: مرام مخارزة

اخي\ اختي المتطوع(ة) هذا البحث هو أحد الابحاث الصحية في مجال الصحة العامة والاوبئة والتي تقوم بها كلية الصحة العامة في جامعة القدس للحصول على درجة الماجستير ويهدف الى دراسة العوامل الاجتماعية والبيئية المحددة لمرض الليشمانيا بنوعيه بين المواطنين الفلسطينيين في محافظتي بيت لحم والخليل.

ارجو ان ابين ما يلي:

ان مشاركتك في هذا البحث تطوعية تماما"، ومن شأنها افادة المجتمع وعملية البحث العلمي بشكل عام.

في حال مشاركتك بالبحث، ستبقى كافة البيانات الشخصية المتعلقة بك سرية تماما، وان كافة البيانات ستستخدم فقط لأغراض البحث العلمي، كما ويحق لك الانسحاب من الدراسة متى شئت من دون أي أثر يذكر عليك.

يجدر الاشارة ان لجنة البحث العلمي في جامعة القدس قد وافقت على اجراء البحث ، وتعتبر هي اللجنة المؤسسية والمرجعية للبحوث والدراسات.

APPENDIX 5: Ethical Approval from The Al-Quds University

Al-Quds University
Jerusalem
School of Public Health

جامعة القدس
القدس
كلية الصحة العامة

التاريخ: 2023/6/24

عزيزتي الطالبة مرام مغارزة المحترمة
برنامج ماجستير الوقاية وضبط الامراض المعدية

الموضوع: موافقة لجنة اخلاقيات البحث العلمي

قامت اللجنة الفرعية لأخلاقيات البحث التابعة لكلية الصحة العامة بمراجعة مشروع الرسالة بعنوان:

"Environmental and social determinants and risk factors for Leishmaniasis in Palestine: A case-control study in Hebron and Bethlehem governorates"

المقدم من (مشرف البحث/د. ياسر عيسى).

يعتبر مشروعك مستوفيًا لمتطلبات أخلاقيات البحث في جامعة القدس.

نتمنى لكم كل التوفيق في تسيير المشروع.

ملاحظة: في حالة الحاجة الى موافقة من اللجنة المركزية في الجامعة، تستطيع التقدم باستخدام هذه الموافقة على الرابط https://research.alquds.edu/en/ethics/48-how-to-apply.html

رئيسة اللجنة الفرعية لاخلاقيات البحث
كلية الصحة العامة
د. نهى الشريف

نسخة/ أعضاء لجنة البحث
نسخة/ الملف

Jerusalem Branch/Telefax 02-2799234
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P.O. box 51000 Jerusalem

فرع القدس / تلفاكس 02-2799234
فرع غزة / تلفاكس 08-264420-2644210
ص.ب. 51000 القدس

العوامل البيئية والاجتماعية المحددة وعوامل الخطر لمرض الليشمانيا الجلدية: دراسة حالة وشواهد في محافظتي الخليل وبيت لحم

الطالبة: مرام المخارزة

المشرف: الدكتور ياسر عيسى

الملخص

الخلفية: يعتبر داء الليشمانيات مشكلة صحية عامة كبيرة في فلسطين، خاصة في محافظتي الخليل وبيت لحم. هدفت هذه الدراسة إلى استقصاء العوامل البيئية والاجتماعية المؤثرة على داء الليشمانيات باستخدام تصميم دراسة الحالة والشواهد (الحالة والعينة الضابطة).

المنهجية والطريقة: تم تضمين ما مجموعه 621 مشاركًا، منهم 207 حالات و414 شاهدًا بنسبة 1:2. تم جمع البيانات باستخدام استبيان شامل يغطي المتغيرات الاجتماعية والديموغرافية، والعوامل البيئية (سواء الداخلية أو الخارجية)، وملكية الحيوانات، وخصائص المنزل، والبيئة المحيطة، والعوامل البيئية الطبيعية (هطول الأمطار ودرجة الحرارة)، والمعرفة حول داء الليشمانيات، والسلوكيات ووسائل الوقاية. تم الحصول على الموافقة الأخلاقية من جامعة القدس، بالإضافة للحصول على الموافقة من جميع المشاركين للمشاركة في الدراسة. تم اختيار عينة الدراسة بطريقة العينة الملائمة البسيطة بناءً على المعلومات المتاحة حول المرضى والتي تم الحصول عليها من وزارة الصحة الفلسطينية، بما في ذلك الأسماء ومعلومات الاتصال. بسبب نقص في معلومات الاتصال، قامت الباحثة وفريقها بزيارة المرضى في أماكن سكناهم. تم تحليل البيانات باستخدام برنامج الرزم الإحصائية للعلوم الاجتماعية (SPSS)، وباستخدام الإحصائيات الوصفية، واختبارات كاي تربيع، وتحليلات الانحدار الأحادية والمتعددة، مع تحديد مستوى الأهمية عند مستوى دلالة احصائية.$p < 0.05$

النتائج: أظهرت التوزيعات المكانية للحالات أن 29.9% منها تركزت في مناطق زعترة، وعرب الرشايدة، والديرات، مع وجود تجمعات ملحوظة في وادي عربة، وديمونا كمصادر للاصابة، وبئر السبع، وإيلات

(16.4%)، وكذلك في مسافر بني نعيم (14.5%). اظهر التحليل الانحداري اللوجستي متعدد المتغيرات عدة عوامل خطرة رئيسية لداء الليشمانيات الجلدي. كان ازدحام المساكن عامل تنبؤ هام، حيث أظهرت الحالات التي تعيش في ظروف مزدحمة زيادة في احتمالية الإصابة (نسبة الأرجحية = 2.10، فترة الثقة 95%: 1.45–3.05). ارتبطت الجودة الرديئة للسكن، التي تتمثل في نقص الصرف الصحي والقرب من مناطق النشاط العالي للناقل، بزيادة في الخطر (نسبة الأرجحية = 2.35، فترة الثقة 95%: 1.50–3.70). كانت الحالة الاجتماعية والاقتصادية المتدنية مرتبطة بشكل كبير بمعدلات الإصابة الأعلى، حيث تأثرت بشكل غير متناسب الأفراد في أدنى فئات الدخل.($p < 0.05$)

كما كانت العوامل البيئية، بما في ذلك هطول الأمطار وطبيعة المنطقة، مهمة أيضًا. وجدت الدراسة أن المناطق التي تتلقى أقل من 300 ملم من الأمطار سنويًا كانت لديها معدلات أعلى لداء الليشمانيات الجلدي، ربما بسبب الظروف الجافة التي تفضل تكاثر وبقاء ذباب الرمل الناقل الأساسي للمرض ($p < 0.05$). أظهر التحليل الطوبوغرافي أن الحالات كانت أكثر شيوعًا في المناطق المنخفضة والوديان، التي توفر مواطن دقيقة مناسبة لذباب الرمل. غالبًا ما تكون هذه المناطق ذات مستويات رطوبة أعلى ونباتات كثيفة، مما يدعم تكاثر الناقلات ويزيد من خطر تعرض الإنسان (نسبة الأرجحية = 1.90، فترة الثقة 95%: 1.30–2.80).

كما واظهرت النتائج ان العوامل السلوكية (سلوكيات الافراد)، وخاصة عادات النوم في الهواء الطلق وعدم كفاية استخدام وسائل الحماية خلال فترات نشاط الناقل في فترات الليل، مرتبطة بشكل كبير بمعدلات إصابة أعلى ($p < 0.01$). واظهرت أيضا ان السكن بالقرب من اماكن الحيوانات والمناطق الزراعية غير المحمية من احتمالية التعرض للدغ ذباب الرمل، الناقل الأساسي لداء الليشمانيات (نسبة الأرجحية = 1.85، فترة الثقة 95%: 1.20–2.85). أظهرت البرامج التعليمية التي تهدف إلى تحسين المعرفة والممارسات المتعلقة بالحماية من الناقلات إمكانات كبيرة كإجراء تدخل، مما يشير إلى أن الوعي العام يعد أمرًا حاسمًا في الحد من انتشار المرض.

الخلاصة: تؤكد النتائج على أهمية تحسين الظروف الاجتماعية والاقتصادية، وتعزيز السكن والصرف الصحي البيئي، وزيادة الوعي حول داء الليشمانيات للحد من انتشار المرض. توصي الدراسة باتخاذ تدابير محددة، بما في ذلك استخدام الناموسيات المعالجة بالمبيدات الحشرية وإدارة أفضل للنفايات لتقليل معدلات العدوى. تعتبر المراقبة المستمرة والاستراتيجيات الصحية العامة المخصصة ضرورية لمعالجة التحدي المستمر لداء الليشمانيات في فلسطين.

الكلمات المفتاحية: داء الليشمانيات، دراسة الحالة والشواهد، العوامل البيئية، العوامل الاجتماعية، فلسطين، الخليل، بيت لحم، الصحة العامة، علم الأوبئة.