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EPIDEMIOLOGICAL STUDY OF LEPROSY IN ELQALAAH DERMATOLOGY AND LEPROSY CLINIC

Thesis

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بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ
قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا
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Engy Mansour Hussein Abdelhameid

List of Contents

List of Abbreviations

Abb.	Full term
BB	*Borderline*
BI	*Bacillary index*
BL	*Borderline lepromatous*
BT	*Borderline tuberculoid*
CAMAS	*Central Agency for Public Mobilization and Statistics*
CMI	*Cell-mediated immunity*
DG	*Dystroglycan*
I	*Indeterminant*
LL	*Lepromatous*
LN	*Laminin*
MB	*Multibacillary*
MDT	*Multi drug therapy*
PB	*Paucibacillary*
PCR	*Polymerase chain reaction*
PGL-1	*Phenolic glycolipid 1*
SD	*Standard deviation*
SPSS	*Statistical Package of Social Science*
TT	*Tuberculoid*
WHO	*World Health Organization*

List of Tables

Page No. Title Table No.

List of Figures

INTRODUCTION

Leprosy has been documented since antiquity. Although it is a curable disease if detected in early stages, it continues to be endemic in some developing countries and a major cause of disability in the world ***(Mathers et al., 2007).***

It primarily affects the skin and peripheral nerves, dependent in large part upon individual's immunologic response to the causative organism, Mycobacterium leprae ***(Bryceson et al., 1990).*** It leads to progressive and permanent damage to the skin, nerves, limbs and eyes. Therefore public education, early diagnosis and the provision of effective treatment with Multi drug therapy (MDT) play an important role in further reducing the stigma linked with the disease ***(Visschedijk et al., 2000).***

The mode of transmission of leprosy is not well understood, although it is probably person to person through nasal droplets ***(Moschella, 2004).*** The disease is classified into two polar forms; tuberculoid and lepromatous, with intermediate (borderline) forms depending on the degree of cell mediated immune response ***(Ridley and Jopling, 1966).*** However, World Health Organization introduced a classification of leprosy into just two groups for practical purposes in the field: paucibacillary leprosy and multibacillary leprosy ***(Belachew et al., 2019).***

In 1981, WHO recommended standard multi-drug therapy against leprosy, and since then the worldwide development of leprosy control activities has been phenomenal ***(Al-Qubati, 2000).*** Despite the free availability and effective utilization of multi-drug therapy worldwide, the decline in newly detected cases over the past decade has been slow; from 249,007 cases in 2008 to 210,671 cases in 2017. The current global annual new case detection rate is 2.7/100,000 population, marginally lower than in previous years (***Palit and Kar, 2020).***

In Egypt, few studies were carried out to study the prevalence of skin diseases. In Assuit, leprosy constituted a significant low prevalence; 0.16% ***(Abdel-Hafez et al., 2003).*** In Cairo, prevalence of all mycobacterial

infections was 0.11% ***(El-Khateeb et al., 2011).*** Such apparent low prevalence was clarified by authors. They stated that unlike hospitals dedicated for management of leprosy in Egypt, their studies were carried out in other hospitals to study all skin diseases, which explains the underestimation of leprosy prevalence. This explanation was clarified by a study carried out in Sohag in a leprosy-specialized hospital, where the prevalence was 3.1 per 100,000 population; close to the worldwide rate ***(EL-Dawela et al., 2012).***

For a decade now, there was no evaluation of the epidemiological trend of leprosy in Egypt. We are in need of updated data about incidence, prevalence and annual case detection rate to support the national strategy of the disease management.

AIM OF THE WORK

The aim of this study is to evaluate the epidemiology of leprosy in Elqalaah leprosy clinic in Cairo over the last 12 years to support the current national control program of leprosy with updated data.

CHAPTER 1

LEPROSY OVERVIEW

Introduction:

Leprosy, also known as Hansen's disease, is a chronic granulomatous disease caused by Mycobacterium leprae ***(Hansen, 1874).*** It mainly affects the skin, the peripheral nerves, mucosa of the upper respiratory tract, and the eyes ***(Sarawad and Mendagudli, 2021).*** Nerve damage may result in lack of ability to feel pain, which can lead to loss of parts of a person's extremities from repeated injuries or infection due to unnoticed wounds. An infected person may also experience muscle weakness and poor eyesight ***(Suzuki et al., 2012).***

Causative organisms:

It is caused by Mycobacterium leprae which is an intracellular, aerobic, pleomorphic, acid-fast, pathogenic bacterium ***(McMurray, 1996).*** Due to its thick waxy coating, Mycobacterium leprae stains with a carbol fuchsin rather than with the traditional Gram stain. Efforts to culture the bacteria in vivo are still under research ***(Gillis, 2015).*** Mycobacterium lepromatosis is a relatively newly identified mycobacterium isolated from a fatal case of diffuse lepromatous leprosy in 2008. Mycobacterium lepromatosis is indistinguishable clinically from Mycobacterium leprae ***(Pushpendra et al., 2016).***

Mode of Transmission:

In 2013, Mycobacterium leprae was identified in the buccal mucosa of 94% of patients presenting with multibacillary and paucibacillary leprosy (PCR analysis and antigenic markers). The main dissemination route of the leprosy bacillus therefore seems to be the upper respiratory tract. ***(Morgado de Abreu et al., 2014).***

The exact route of transmission of Mycobacterium leprae in humans has not yet been sufficiently elucidated. To date, humans affected by

leprosy are considered to be the only source of infection. The most important mode of transmission is droplet infection via the nasal mucosa, which is followed by the development of a localized primary lesion, similar to tuberculosis. However, transcutaneous transmission following direct skin contact with untreated, ulcerated, multibacillary lepromatous nodules is also thought to be a possible transmission pathway ***(Fischer, 2017).***

Several predisposing factors for transmission of Mycobacterium leprae are thought to have been confirmed by now, including close and prolonged contact with an infected individual with a high bacterial load. In this context, patients with lepromatous leprosy are considered to be most contagious. Apart from exposure, the individual immunocompetence of an infected person determines whether clinical infection will develop following transmission ***(Fischer, 2017).***

Pathogenesis:

Mycobacterium leprae has predisposition to infect macrophages. It is usually collected inside these, in intracellular groups, called globi. This organism has an ideal growth temperature of 27-30ºC, which explains why it usually infects areas such as the skin, upper respiratory mucosa and peripheral nerves. It is able to infect cells, particularly due to two structures which are the capsule and the cell wall ***(Eichelmann et al., 2013).***

The bacillus invades Schwann cells by binding to the alpha (α)-dystroglycan of Schwann cells via the interaction of α-DG and laminin–α2 in the basal lamina that surrounds the Schwann cell-axon unit in the peripheral nerves. Thereby explaining the neuropathy felt in this condition ***(Jin et al., 2019).***

This mechanism explains the reason why the clinical manifestations of the disease will depend on the immunologic status of the patient and the intensity of the response developed following the infection of the host cells ***(Eichelmann et al., 2013).***

Classification:

Ridley-Jopling classification:

This is a histological classification scheme for leprosy that ranged in severity, beginning with early indeterminant (I) leprosy and continuing with polar tuberculoid (TT) leprosy, borderline tuberculoid (BT) leprosy, mid-borderline (BB) leprosy, borderline lepromatous (BL) leprosy, and polar lepromatous (LL) leprosy. In the tuberculoid form there is heightened cell-mediated immunity (CMI), whereas in the lepromatous form there is an increased humoral immunity ***(Ridley and Jopling, 1966).***

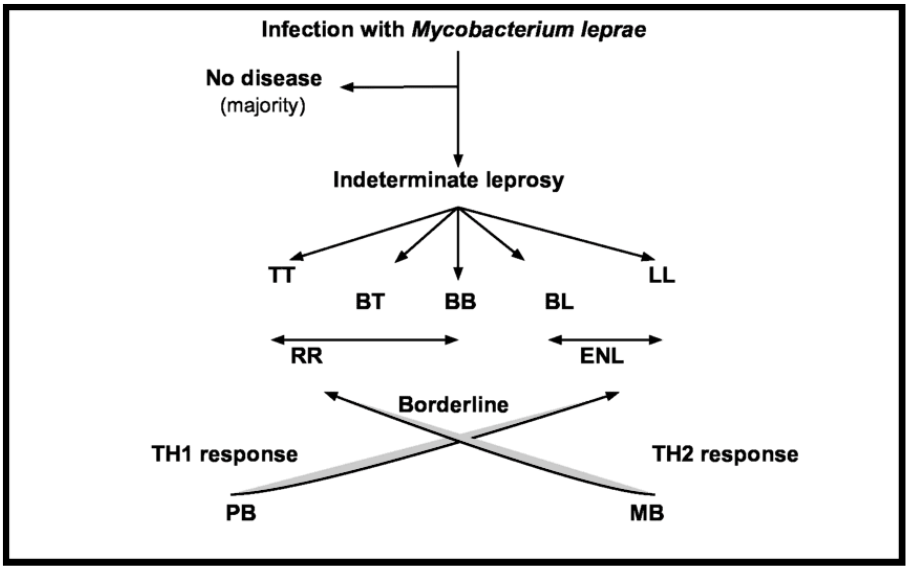

Figure (1): The Ridley-Jopling classification of leprosy
(Ridley and Jopling, 1966).

WHO classification:

In 1998, WHO's Expert Committee on Leprosy determined that treatment could be started before smear tests were done; thus, a practical, rapid classification was established depending on skin lesions with sensory loss with or without positive skin smears for worldwide application without need for diagnostic equipment and without putting health care workers at risk ***(Bakker et al., 2004).***

- Multibacillary Type: more than 5 skin lesions
- Paucibacillary Type: one to 5 skin lesions ***(Moschella, 2004).***

Multibacillary Type includes LL, BL and BB forms and paucibacillary Type includes the TT and BT forms of the Ridley-Jopling classification system.

Clinical features:

In each type one or more of four sites may be affected:

- Nerves
- Dermis (skin)
- Mucosa
- Internal organs

Nerve affection:

Nerve involvement is found in all forms and may also occur in the absence of skin lesions ***(Talhari et al., 2015).*** That is because it is one of the most common infectious diseases associated with the peripheral nervous system and frequently results in disability if early treatment is delayed. Thus, the early recognition and prompt treatment of neural involvement is of paramount importance. Nerve function impairment at initial presentation is common and occurs at rates as high as 55% ***(Saunderson, 2000)***.

The first neurological manifestation is often the development of sensory loss or paraesthesias in one or more cutaneous skin patches. A patient mounting a good cellular response, such as that seen in TL, typically will have a mononeuropathy or mono-neuritis multiplex. The nerves commonly involved in TL are the superficially located nerves, such as the ulnar and the common peroneal nerve, where it has been postulated that the cooler temperatures of these regions favor bacterial proliferation. Those with LL and the corresponding heavy bacterial load have more diffuse involvement of the peripheral nerves and often present with a symmetrical polyneuropathy ***(Vijayan and Wilder-Smith, 2016).***