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The demographic and clinical characteristics of leprosy in Saudi Arabia

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Summary Leprosy is a chronic disease caused by Mycobacterium leprae. Although the occurrence of leprosy has declined in Saudi Arabia, it has not yet been eradicated. To our knowledge, this descriptive retrospective study is the first to assess the clinical presentation of leprosy at the time of diagnosis in Saudi Arabia. All study subjects were leprosy patients admitted to Ibn Sina hospital, the only referral hospital for leprosy in Saudi Arabia, between January 2000 and May 2012. A total of 164 subjects, the majority of whom (65%) were between 21 and 50 years of age, were included, and the male-to-female ratio was 2.8:1. Of these 164 patients, 63% were Saudis, and 77% of all admitted patients were from the western region. Lepromatous leprosy was observed most frequently (33%), and 31% of cases had a positive history of close contact with leprosy. At the time of diagnosis, 84% of all subjects presented with skin manifestation. The prevalence of neurological deficit at the time of diagnosis was 87%. Erythema nodosum leprosum (E.N.L.) developed in only 10% of all subjects. Further studies are needed to determine the clinical characteristics pertaining to each type of leprosy in the region, and training courses in caring for and diagnosing patients with leprosy should be organized for health workers.

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Introduction

Leprosy is a chronic disease caused by Mycobacterium leprae [1]. M. leprae is similar to Mycobacterium tuberculosis, although it is resistant to culture [1]. It is an intracellular microbe that prefers to infect cooler areas of the human body, including the skin and nerves [2]. Dermatological lesions and peripheral neuropathy are the cardinal clinical features of leprosy [1]. Most cases of leprosy have been reported in developing countries [1]. Leprosy is a curable disease if detected in early stages, and early detection is critical for the prevention of disabilities [1]. In the United States, approximately 75% of new cases were detected in immigrants in 2010 [3]. Most leprosy patients in the USA were affected by lepromatous leprosy [3]. Of diagnosed leprosy patients in Saudi Arabia, 57% are immigrants, and leprosy is more common in males than females at a ratio of 3—1 [4]. Regarding the epidemiology in Saudi Arabia, Assiri et al. reported the occurrence of 242 new leprosy cases over a 10-year period spanning 2003—2012 [4]. The risk of leprosy was higher in older individuals. In one study, the risk of contracting the disease was found to increase between the ages of 5 and 15 years and increased again after the age of 30 [5]. The disease is transmitted from one person to another through close contact [6], which in the case of leprosy, may mean skin-to-skin contact or exposure to a patient's oral droplets [7]. Some studies have suggested that patients with a history of contact with multibacillary leprosy have a higher risk than patients in contact with paucibacillary leprosy [6]. The disease is thought to be transmitted through nasal discharge, but the exact mechanism of transmission is not fully understood [8].

According to the Ridley and Jopling classification system, there are five types of leprosy: lepromatous (LL), tuberculoid (TT), borderline borderline (BB), borderline lepromatous (BL) and borderline tuberculoid (BT) [9]. Ridley and Jopling have also used the term indeterminate leprosy (IL) [10] when a biopsy sample shows evidence of leprosy without a clear clinical manifestation [10]. Patients with evidence of neurological deficits or damage without any skin manifestations are considered to have pure neural leprosy [11]. Another classification system for leprosy was developed by the World Health Organization (WHO). The WHO divides leprosy into two types: paucibacillary (includes TT, BT and IL) and multibacillary (includes LL, BL and BB) [12]. There are two types of systemic reactions to leprosy. Type 1 reactions (i.e., reversed reactions) occur in patients with borderline leprosy (i.e., borderline borderline, borderline lepromatous and borderline tuberculoid), whereas type 2 reactions (i.e., erythema nodosum leprosum or ENL) occur in patients with lepromatous and borderline lepromatous leprosy [2]. ENL presents with red painful nodules on the skin, which mostly develop later in the course of the disease [13]. The management of ENL compromises prolonged courses of prednisolone [13]. If the disease is severe, then thalidomide may be used [14]. The aim of this study is to determine the demographics of patients admitted with a diagnosis of leprosy and to assess and compare neurological deficit (e.g., sensory or motor loss, nerve enlargement or anesthetic lesion,), skin manifestation (e.g., hypopigmented lesions, plaque or macule) and erythema nodosum leprosum in various leprosy types in Saudi Arabia. Because of the need for clinical indicators to aid primary healthcare physicians in the early detection of the disease, we focused our efforts on quantifying the types and characteristics of leprosy found in Saudi Arabia. To our knowledge, this is the first study to assess the clinical presentation of leprosy at the time of diagnosis in Saudi Arabia.

Methodology

This is a descriptive retrospective study. The subjects of this study were all patients diagnosed with leprosy at Ibn Sina Hospital between January 2000 and May 2012. The study was conducted in Ibn Sina Hospital, which is a leprosy referral hospital in the Makkah region. In total, 164 subjects were enrolled. Twelve subjects were excluded from our study due to insufficient file information.

Patient information and data, including age, sex, nationality, area of residence, year of registry, type of the disease and signs and symptoms at the time of diagnosis, were collected from the patients' files. The data were categorized according to the Ridley and Jopling classification [9]. The diagnosis of leprosy was based on clinical manifestations in addition to a skin smear, which was obtained for all patients and examined in a laboratory to determine the type of leprosy. The data were transferred to coding sheets and were entered into an Excel file. The data were analyzed using SPSS version 16. Qualitative variables are categorized and presented as frequencies and percentages. Quantitative variables are presented as the mean and standard deviation. Categorical variables were compared using the chi-square test, odds ratio and a 95% confidence interval. A P value <0.05 was considered significant. Openepi, which is a free web-based statistical program, was used to calculate the P value, odds ratio and confidence

interval [15] in conjunction with SPSS version 16. Approval for the study was obtained from the director of health affairs in Makkah. All subjects were anonymized during data entry.

Results

In this study, we considered patients diagnosed with leprosy at Ibn Sina Hospital from January 2000 to May 2012. We enrolled a total of 164 subjects after excluding patients with incomplete files. Of these subjects, the majority of patients (65%) were between 21 and 50 years old. Subjects over 50 years old comprised 31% of the cohort, and only seven (4%) of the subjects were under 20 years old. The mean age of the study group was 43.24 + 17.1, and the male-to-female ratio was 2.8:1 [121 subjects (74%) were male and 43 (26%) were female]. Of the 164 reported patients, 103 (63%) were Saudis. The majority of patients — 127 (77%) — were from the western region. The southern region had the second largest number of cases at 31 (19%). The number of patients reported from northern region was three (2%), while two were reported from the central region (1%) and one (1%) was from the eastern region. These data indicate that the disease may be concentrated in the western region of Saudi Arabia (Table 1).

Using Ridley and Jopling's classification system, lepromatous leprosy affected the highest number of infected subjects [54 (33%)]. The number of subjects affected by the other types were as follows: borderline tuberculoid leprosy, 42 (26%); tuberculoid leprosy, 26 (16%); borderline borderline leprosy, 22 (13%); borderline lepromatous leprosy, 13 (8%); pure neural leprosy, five (3%); and indeterminate leprosy, two (1%) (Table 2).

There was a positive history of close contact, skin-to-skin contact, exposure to a patient's oral droplets or prior leprosy in 31% of cases. Specifically, three (60%) of the subjects exhibited pure neural leprosy, 11 (42%) tuberculoid leprosy, 14 (33%) borderline tuberculoid leprosy, four (31%) borderline lepromatous leprosy, 16 (30%) lepromatous leprosy and three (14%) borderline borderline leprosy. In contrast, none of the patients with indeterminate leprosy reported close contact history. In accordance with WHO classification, we excluded five subjects who had been diagnosed with pure neural leprosy, which is not included in the WHO system. This criterion resulted in the inclusion of 159 subjects rather than 164 in this comparison. Of patients with Multibacillary leprosy, 23 (26%) reported a close contact history, while 25 (36%) patients with Paucibacillary leprosy reported close contact (Table 3).

Regarding clinical presentation at the time of diagnosis, 84% of our subjects presented with skin manifestation. Borderline borderline leprosy was most frequently associated with skin manifestation, with 96% of patients presenting with this feature. Borderline lepromatous followed with 92%, lepromatous with 91%, borderline tuberculoid with 86% and tuberculoid with 65%, with clinically significant differences ($P < 0.05$). Finally, pure neural leprosy never presented with skin manifestation ($P < 0.05$). Although pure neural leprosy does not present with skin manifestation at the time of diagnosis, such symptoms may develop over time, as leprosy is highly unpredictable [16]. It is worth mentioning that our indeterminate subjects (100%) presented with skin manifestation at the time of diagnosis (Table 4).

In total, 87% of subjects presented with a neurological deficit at the time of diagnosis All subjects who were diagnosed with tuberculoid or pure neural leprosy had neurological symptoms (100%). Borderline lepromatous patients followed at 92%, then borderline borderline at 91%. Borderline tuberculoid and lepromatous patients were affected in 86% and 80% of cases, respectively. Lepromatous patients exhibited a clinically significant difference at $P < 0.05$. Finally, one subject with indeterminate leprosy (50%) had neurological deficits (Table 5).

Table 6 shows that ENL developed in only 10% of all subjects. It was significantly associated with borderline lepromatous leprosy, as 46% of these patients developed ENL ($P < 0.001$). There was also a significant association between ENL and lepromatous leprosy, as 19% of patients developed the complication ($P < 0.05$). One subject diagnosed with borderline borderline leprosy (5%) developed ENL, while the rest of the types did not exhibit any involvement of ENL.

Discussion

Leprosy is one of the oldest diseases known to mankind [17]. Its prevalence has been in decline worldwide at least since the first Leprosy Expert Committee meeting of the WHO in 1956 [18]. Nevertheless, there remain endemic areas affected by leprosy, such as India and Indonesia [19]. The disease is known to exist in Saudi Arabia [20], and although the exact number of infected patients is not precisely known, it does not pose a public health problem. Assiri et al. reported a total of 242 infected residents in Saudi Arabia nationwide over a 10-year period (2003—2012) [4]. In our study, we focused on leprosy patients admitted to the Ibn Sina Hospital, which is the only referral center

for leprosy in the country. A total of 164 patients were treated over a 12-year period. Although more patients were admitted to Ibn Sina Hospital during this time, 12 subjects were excluded from our study due to insufficient file information. It is believed that the number of leprosy patients in Saudi Arabia is greater than is reported because leprosy is stigmatized in society; we may not be able to precisely account for all leprosy patients in Saudi Arabia because many travel abroad for treatment [21]. The total number of Saudis worldwide with leprosy has not yet been described in the literature. New cases must be self-reported by patients, as there are no surveillance studies [21]. The non-specific clinical presentation, the lack of involvement of structures other than skin and peripheral nerves, the long incubation period of the disease, and its atypical clinical presentations all make the diagnosis of leprosy challenging, especially in non-endemic countries [22]. Nevertheless, there has been a decline in the incidence of leprosy in Saudi Arabia [4].

Atypical forms of the disease have been reported in the literature, and the emergence of newer forms can lead to a delay in diagnosis [23]: an estimated 82% of leprosy cases are misdiagnosed in the UK [22]. Thus, there is a need to identify clinical indicators to aid in the early detection of the disease. To this end, we focused our efforts on quantifying the types of leprosy found in Saudi Arabia and their characteristics according to the Ridley and Jopling classification rather than the WHO classification, as well as adding pure neural leprosy as a separate class. The majority of our subjects were afflicted with lepromatous leprosy (33%). To compare our results with those of Assiri et al., we utilized the WHO classification system. Assiri et al. reported that the majority of cases were PB (50.8%) [4]. In our study, PB accounted for 43% of leprosy patients in Ibn Sina Hospital, most of which were borderline tuberculoid (26%), while 54% had MB and only 3% had pure neural leprosy. In our study, MB was the most common type of leprosy.

Furthermore, a huge number of non-Saudis — particularly from India and Indonesia, known endemic areas for leprosy — come to Saudi Arabia for religious reasons or for work [19] and may have inactive or undiagnosed leprosy. This is in line with the findings of Al-Mutairi et al., who reported that 73.9% of leprosy cases in Kuwait originated in India and its neighboring countries [24]. Our findings suggest that only 37% of patients were non-Saudis. This may be because foreigners diagnosed with leprosy are treated for one month and then are sent back to their home country [4]. To compare immigrants in Saudi Arabia, Assiri et al. reported that 57.4% of cases were non-Saudis [4]. As expected, males are affected more frequently with the disease than females, with a male-to-female ratio of 2.8:1. This is consistent with studies conducted in Saudi Arabia and elsewhere [4,21], which indicate ratios ranging from 3.4:1 to 3.83:1 [4,20]. In addition, the geographical distribution of the disease confirmed the results of previous studies conducted in Saudi Arabia. Al Aboud et al. reported that 45% of leprosy patients came from the western region of Saudi Arabia [21]. Makkah had the highest number of cases, representing 42% of all reported cases in Assiri et al.'s study [4]. Our study indicated that 77% of subjects were from the western region. We found that the second highest region of leprosy cases was the Southern region, with 19%. However, according to Assiri et al., the second highest incidence of leprosy was the eastern region, with 20% of cases [4]. Only 1% of our subjects were from the eastern region. This could be due to the geographical location of Ibn Sina Hospital in the western region. Furthermore, we found that a history of close contact was prominent in patients with PB leprosy, which is contrary to other reports in the literature [6]. This may be due to the subjective approach of the diagnosing physician when taking a history at the time of diagnosis. Rodrigues et al. stated that the risk of infection is almost doubled for MB compared to PB [25]. Interestingly, there is no skin manifestation for patients with pure neural leprosy at the time of diagnosis, although it may develop in later stages [26]. This illustrates the unpredictable presentation of leprosy [16].

Tuberculoid leprosy is known to present with a neurological deficit at diagnosis [27,28]. This was observed in our subjects; all patients with tuberculoid leprosy (100%) exhibited some form of neurological deficit. In cases of lepromatous leprosy, neurological deficits are less likely to be present at the time of diagnosis, but can occur in later stages [26]. The prevalence of neurological deficit was 80% in our subjects diagnosed with lepromatous leprosy. ENL is a rare complication of leprosy in general, but as expected, was a common complication in lepromatous leprosy and borderline lepromatous leprosy [2,26,27,29]. Out of all 164 subjects, only 17 (10%) developed ENL, 10 of which were affected by lepromatous leprosy and six of which had borderline lepromatous leprosy.

Conclusion/Recommendation

Although leprosy is not a major public health problem in Saudi Arabia and the number of reported

cases has decreased over the past several years, it has not been eradicated. Leprosy cases are concentrated in the western and southern regions. Our study describes the demographics and the pattern of clinical presentation of different types of leprosy. Further studies are needed to investigate the clinic characteristics pertaining to each type of leprosy in the region because it is important to diagnose the disease in its early stages to prevent complications. Training courses should be organized for health workers involved in caring for patients with leprosy, including dermatologists, microbiologists and physiotherapists. Courses on the diagnosis of leprosy should be organized for primary healthcare physicians.

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Competing interests

None declared.

Ethical approval

The study was approved by the director of health affairs in Makkah.

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Appendix.

Table 1 Demographic data of patients with leprosy in Saudi Arabia (January 2000—May 2012).

Demographic items				Total	%
Age mean	43.24 ± 17.1				
Age range (years)	**Frequency (*n*)**		**%**		
	<20	7	4		
	21—50	106	65		
	>50	51	31		
Sex	Male	121	74		
	Female	43	26		
Nationality	Saudi	103	63		
	Non-Saudi	61	37	164	100
Region	Northern	3	2		
	Southern	31	19		
	Western	127	77		
	Eastern	1	1		
	Central	2	1		

Table 2 Classification of leprosy in patients reported in Saudi Arabia (2000—2012).

Type of disease	Frequency (*n*)	%
Lepromatous	54	33
Tuberculoid	26	16
Borderline borderline	22	13
Borderline tuberculoid	42	26
Borderline lepromatous	13	8
Pure neural	5	3
Indeterminate	2	1
Total	164	100

Table 3 The association between the type of leprosy and the close contact history with the disease among Saudi patients (2000—2012).

Type of leprosy (Ridley and Jopling classification)	Close contact ($n = 164$)		Total (%)	*P*-value
	Yes ($n = 51$)	No ($n = 113$)		
Lepromatous	16 (30)	38 (70)	54 (33)	0.77
Tuberculoid	11 (42)	15 (58)	26 (16)	0.17
Borderline borderline	3 (14)	19 (86)	22 (13)	0.057
Borderline tuberculoid	14 (33)	28 (67)	42 (26)	0.71
Borderline lepromatous	4 (31)	9 (69)	13 (8)	0.97
Pure neural	3 (60)	2 (40)	5 (3)	0.15
indeterminate	0 (0)	2 (100)	2 (1)	>0.99*
Type of leprosy (WHO classification)	Close contact ($n = 159$)		Total (%)	*P*-value
	Yes ($n = 48$)	No ($n = 111$)		
Multibacillary (MB)	23 (26)	66 (74)	89 (54)	0.18
Paucibacillary (PB)	25 (36)	45 (64)	70 (43)	0.18

* Fisher exact test.

Table 4 The association between the type of leprosy and skin manifestation in Saudi Arabia (2000—2012).

Type of leprosy	Skin manifestation ($n = 164$)		Total (%)	*P*-value	Odds ratio	95% C.I.
	Yes ($n = 137$)	No ($n = 27$)				
Lepromatous	49 (91)	5 (9)	54 (33)	0.08	2.45	0.87, 6.87
Tuberculoid	17 (65)	9 (35)	26 (16)	<0.05	0.28	0.11, 0.73
Borderline borderline	21 (96)	1 (4)	22 (13)	0.10	4.70	0.60, 36.60
Borderline tuberculoid	36 (86)	6 (14)	42 (26)	0.65	1.24	0.47, 3.33
Borderline lepromatous	12 (92)	1 (8)	13 (8)	0.37	2.50	0.31, 20.04
Pure neural	0 (0)	5 (100)	5 (3)	<0.05*	0.038	0.0007, 0.38
Indeterminate	2 (100)	0 (0)	2 (1)	>0.9*	0.62	0.025, 47.93

* Fisher exact test.

Table 5 The association between the type of leprosy and neurological deficits in Saudi Arabia (2000—2012).

Type of leprosy	Neurological deficits ($n = 164$)		Total (%)	*P*-value	Odds ratio	95% C.I.
	Yes ($n = 143$)	No ($n = 21$)				
Lepromatous	43 (80)	11 (20)	54 (33)	<0.05	0.39	0.15, 0.99
Tuberculoid	26 (100)	0 (0)	26 (16)	0.21*	4.31	0.62, 186.9
Borderline borderline	20 (91)	2 (9)	22 (13)	0.57	1.54	0.33, 7.14
Borderline tuberculoid	36 (86)	6 (14)	42 (26)	0.73	0.84	0.30, 2.33
Borderline lepromatous	12 (92)	1 (8)	13 (8)	0.56	1.83	0.22, 14.86
Pure neural	5 (100)	0 (0)	5 (3)	>0.99*	1.15	0.095, 73.4
Indeterminate	1 (50)	1 (50)	2 (1)	0.11	0.14	0.008, 2.34

* Fisher exact test.

Table 6 The association between the type of leprosy and erythema nodosum leprosum in Saudi Arabia (2000—2012).

Type of leprosy	E.N.L. ($n = 164$)		Total (%)	*P*-value	Odds ratio	95% C.I.
	Yes ($n = 17$)	No ($n = 147$)				
Lepromatous	10 (19)	44 (81)	54 (33)	<0.05	3.34	1.20, 9.35
Tuberculoid	0 (0)	26 (100)	26 (16)	0.40*	0.30	0.007, 2.11
Borderline borderline	1 (5)	21 (95)	22 (13)	0.34	0.37	0.047, 3.002
Borderline tuberculoid	0 (0)	42 (100)	42 (26)	0.06*	0.16	0.003, 1.09
Borderline lepromatous	6 (46)	7 (54)	13 (8)	<0.001	11	3.12, 38.12
Pure neural	0 (0)	5 (100)	5 (3)	0.9*	1.98	0.039, 20.24
Indeterminate	0 (0)	2 (100)	2 (1)	0.48*	5.90	0.087, 142.7

* Fisher exact test.

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