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CASE REPORT

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Leprosy – neglected tropical disease in Pygmies inhabiting Central African Republic

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Abstract

Leprosy is a neglected tropical disease that is still present worldwide despite efforts aimed at elimination of the disease. The BaAka Pygmy community inhabiting rural areas in the Central African Republic is one of the most leprosy-vulnerable populations. The aim of the study was to assess the prevalence of leprosy in the BaAka Pygmy population. People living in the Dzanga Sangha protected area were regularly visited by a mobile clinic in 2019/2020. The diagnosis was based on the clinical manifestation of the disease. Deformations of skin and extremities were assessed. In a 12-month period 26 cases of leprosy were diagnosed and 25 patients received treatment. 24 of those patients were BaAka Pygmies, 10 were women, 7 were children under 15 years old and 8 were diagnosed with grade 2 disability. Presented data shows that leprosy in Dzanga Sangha region is not well controlled due to the high transmission rate. Efforts to diagnose and report new leprosy cases should be intensified.

Key words

Mycobacterium leprae, Central African Republic, leprosy, BaAka Pygmies

Abbreviations

DS – Dzanga Sangha; **CAR** – Central African Republic; **WHO** – World Health Organization; **MDT** – Multidrug therapy; **MB** – multibacillary; **PB** – paucibacillary; **G2D** – Grade 2 Disability

INTRODUCTION

The fight against leprosy on a global scale was initiated a half a century ago [1], but today leprosy is recognized as one of the neglected diseases. References to the disease can be found in ancient sources [2] dating back thousands of years, and in some societies even today, the disease was considered a curse, a punishment for sins, and people suffering from leprosy were isolated and excluded from society [3, 4].

The etiology of the disease remained unknown until the discovery in 1873 by Armauer Hansen, a the Norwegian scientist, of the rod-shaped Gram-positive bacterium *Mycobacterium leprae* [5, 6]. In 2008, a second type of mycobacterium causing leprosy was discovered in Mexico. The newly-discovered *Mycobacterium lepromatosis* [7] shows a similarity of 87–93% to the *M. leprae* genome [7, 8, 9]. Although they might have common clinical manifestation, it was observed that *M. lepromatosis* causes more diffuse forms [10, 11]. The disease is present worldwide and affects all six continents, although the vast majority of cases are reported in Southeast Asia (Fig. 1).

Since 1981, the World Health Organization (WHO) has recommended the use of a combination treatment known as the multidrug therapy (MDT) with dapsone, rifampicin and clofazimine which are provided to patients free of charge [1]. Originally, the treatment regimens were based on the Ridley-Joplin classification which defined six manifestations of leprosy with two polar-tuberculoid and lepromatous-based on the bacterium index load in the skin smears. In 1993, the WHO simplified the classification criteria and created a clinical classification model that has direct implications for treatment. According to this classification, there are two main types of leprosy: the paucibacillary (PB) and the multibacillary (MB). Patients presenting with less than six skin lesions are classified as having the less infectious PB leprosy and are given six-month MDT, while patients with six and more skin lesions are classified as having highly infectious MB leprosy. In such cases the minimum duration of MDT is 12 months [13].

Leprosy is considered as a significant public health problem, and there have been several attempts to eliminate the disease, but so far efforts have been unsuccessful [14]. The disease is transmitted by the aerosol route – through infected droplets excreted when an infected person coughs or sneezes, although some types of leprosy can also be transmitted through prolonged contact with the skin lesions of an infected person [1].

As both humans and nine-banded armadillos (*Dasypus novemcinctus)* can carry the same strains of leprosy-causing bacteria, transmission of leprosy from these animals cannot be ruled out [15]. In addition, in 2016, *M. leprae* were detected in red squirrels (*Sciurus vulgaris*) living in the British Isles [15, 16], although their role in the zoonotic disease transmission onto humans is questionable [17]. Poor hygiene

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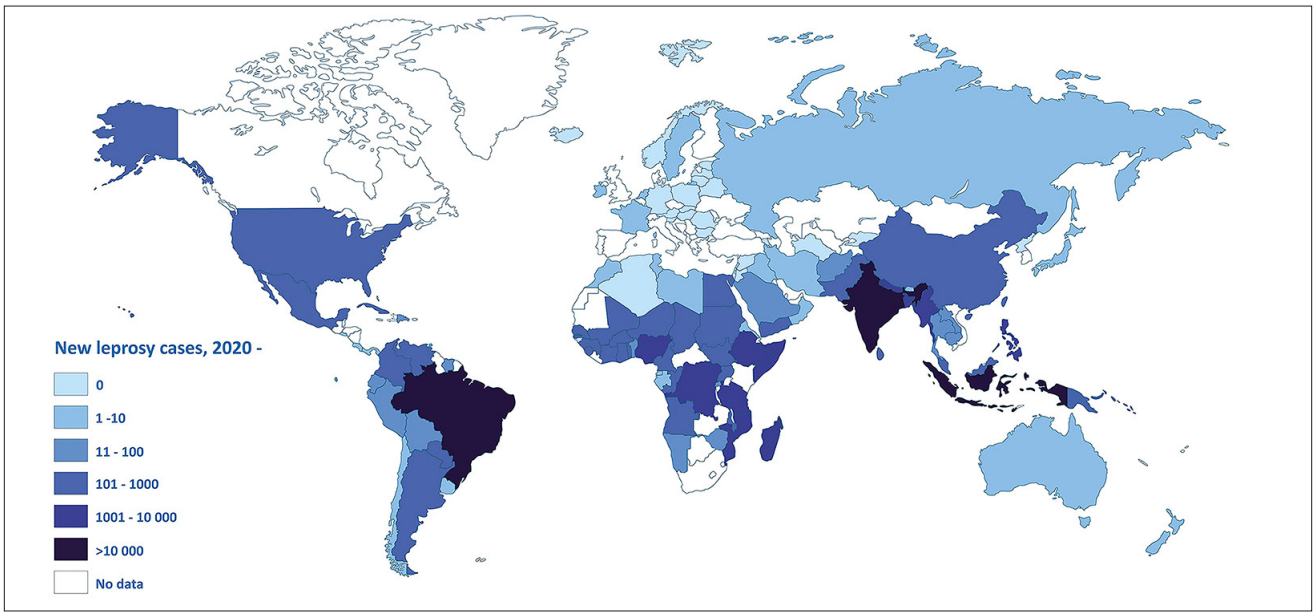

Figure 1. Distribution of new leprosy cases in 2020 according to WHO data [12]

and close contacts with people who have leprosy favour the transmission of the disease which develops slowly, and symptoms may appear many months or even years after infection [1]. The disease mostly affects the skin, the nerves, the mucosa of the upper respiratory tract, and the eyes; also, more rarely, the testicles and bones [3].

In 2019, the Central African Republic (CAR) reported 343 new cases, however, there is no data available for cases undergoing treatment and supervision of treatment. Because of their hunter-gatherer lifestyle, limited trust in local health professionals and the lack of education, BaAka Pygmies rarely appear in official leprosy records and are not covered with the leprosy treatment. The BaAka Pygmy population also has very limited access to health care due to their limited financial resources [18]. Moreover, due to political instability in the CAR since 2012, with the most intense conflict taking place between 2013 – 2015 [19, 20], both patients' access to medical care and access to MDT were seriously limited or absent, as evidenced by the WHO statistics [21]. The lack of data in many fields is due to the lack of reporting (Tab. 1).

OBJECTIVE

The aim of the study was to assess the prevalence of leprosy in the BaAka Pygmy population inhabiting the rural and forest areas of the Dzanga Sangha protected area in the CAR, to improve the availability of leprosy treatment, and prepare a report to be used for the development of future health projects in this area.

MATERIALS AND METHOD

In 2019–2020, the villages inhabited by BaAka Pygmies and Bantu people, located in the protected area of the Dzanga Sangha region in southwestern CAR, were regularly visited by a mobile clinic offering medical consultations. Age, gender and patient's ethnicity were noted. The diagnosis of leprosy was based on the clinical symptoms. The number and location of skin lesions with reduced sensation to touch were assessed according to the WHO clinical 'field-friendly'

Table 1. Leprosy statistics in CAR in the years 2012–2020

	2012	2013	2014	2015	2016	2017	2018	2019	2020
Number of new leprosy cases	152	99	68	No data	385	341	173	343	No data
New leprosy case detection rate per 1 000 000 population	33.59	21.445	14.44	No data	83.794	73.19	37.074	72.284	No data
Number of leprosy cases registered for treatment (prevalence)	256	154	178	No data	385	118	No data	No data	No data
Leprosy registered prevalence rate per 1 000 000 population	56.572	33.359	37.798	No data	83.794	25.327	No data	No data	No data
Number of new leprosy cases with G2D	22	8	9	No data	13	0	No data	No data	No data
Proportion of new leprosy cases with G2D	14.5	8.1	13.2	No data	3.4	0	No data	No data	No data
New leprosy cases with G2D per 1 000 000 population	4.899	1.778	1.993	No data	2.829	0	No data	No data	No data
Number of new leprosy cases among children (<15 years)	19	14	14	No data	43	58	No data	57	No data
New leprosy child detection rate (<15 years) per 1 000 000 child population	9.576	6.718	7.196	No data	21.784	29.215	No data	27.35	No data
Number of new leprosy cases with G2D among children (<15 years)	-	-	No data	No data	5	0	No data	No data	No data
Proportion of children (<15 years) among new leprosy cases	12.5	14.1	20.6	No data	11.2	17	No data	16.6	No data
Number of new leprosy cases among females	70	38	31	No data	67	77	No data	No data	No data
Proportion of females among new leprosy cases	46.1	38.4	45.6	No data	17.4	22.6	No data	No data	No data

classification [22]. Distinguishing between PB and MB leprosy was based on the number of lesions. Patients with typical leprosy manifestations were given MDT, administered according to WHO recommendations and type of leprosy. Uncertain cases were consulted with the national specialist on leprosy. Neither the examination of the peripheral nerves in search of thickening or soreness, nor the assessment of vision impairment were performed. Skin slit-smears were not taken, nor were skin biopsies performed due to the absence of laboratory facilities and competent laboratory technicians within 500 kilometres of the Dzanga Sangha district who would be able to perform the tests. The villages in the region were visited regularly every two to four weeks. At the control visits, the continuation of MDT was distributed and follow-up was performed for some patients. All cases were reported to local health authorities for statistic purposes and MDT obtainment.

Photographs of lesions were taken after informed oral consent by the patient. Consent to participate in the study was obtained from parents/guardians of paediatric patients.

RESULTS

From February 2019 – February 2020, while the mobile clinic was visiting surrounding villages in the Dzanga Sangha region, leprosy was found in 26 people of whom 24 were BaAka Pygmies. The largest leprosy outbreak was found in Lindjombo village located on the extreme south-west of the CAR, on the border with Cameroon, where BaAka Pygmies households accounted for 45% of all households. A total of 13 patients came from Lindjombo, among whom there were 12 BaAka Pygmies and 1 Bantu person [23]. The location of the skin lesions varied between patients (Tab. 2). Multiple lesions dominated and were found in 22 patients vs. single lesions found in only three patients. The most common locations of the lesions were the face and the feet – nine patients in both cases, the back – eight patients, the arms – 7 patients, and the hands, lower limbs and buttocks – six patients each location.

Case statistics, according to the WHO clinical leprosy classification[13, 22], are shown in Table 3. The vast majority of new leprosy cases were MB leprosy manifestations, found in 16 adults, including seven women and three children aged under 15. PB leprosy manifestations with up to five skin lesions were found in seven adults, including two women and three children under the age of 15. PB leprosy manifestations with a single lesion were found in three adults, including one woman and one child under 15 years old.

Among 24 BaAka Pygmies diagnosed with leprosy, the MB manifestations were found in 15 patients. Nine BaAka patients presented PB manifestations, of whom two were diagnosed with a single leprosy lesion. Of the two Bantu patients diagnosed with leprosy, one was diagnosed with PB leprosy and one with the MB manifestation of the disease.

Table 2. Location of the skin lesions in leprosy patients in Dzanga Sangha region

	Single lesion	Multiple lesions
Ear lobe	0	5
Face	0	9
Hairy scalp skin	0	1
Neck	0	1
Shoulders	0	8
Abdomen	0	3
Hands	0	6
Forearms	0	3
Arms	0	7
Feet	1	9
Legs	1	6
Thighs	1	2
Buttocks	0	6

Table 3. Number of leprosy cases in Dzanga Sangha region according to the WHO clinical classification

	Paucibacillary single lesion leprosy: 1 skin lesion	Paucibacillary leprosy: 2 to 5 patches or lesions on the skin	Multibacillary leprosy: >5 patches or lesions on the skin
Adults (all cases)	3	7	16
Women	1	2	7
Children (<15 years)	1	3	3
BaAka	2	7	15
Bantu	1	0	1

Table 4 presents the data collected by personnel of a mobile clinic during a 10-month period, from February 2019 – December 2019, in the Dzanga Sangha region of the CAR. For statistical comparative analysis, only new leprosy cases from 2019 were considered, 25 new leprosy cases were found, of which 24 started MDT. One person refused treatment due to alcohol addiction. Of the 25 new cases, seven were found in children between the ages of four and 14 years. Disfigurement for characteristic to G2D was found in eight patients, including one child under the age of 15. Ten out of the 25 new leprosy cases were women. In January 2020, one BaAka woman was diagnosed with leprosy and treated with MDT.

Table 4. Leprosy cases in Dzanga Sangha region, CAR in 2019

	Dzanga Sangha Mobile Clinic Data 2019
Number of new leprosy cases	25
Number of leprosy cases registered for treatment (prevalence)	24
Number of new leprosy cases with Grade 2 Disability (G2D)	8
Proportion of new leprosy cases with G2D (%)	32
Number of new leprosy cases among children (<15 years)	7
Number of new leprosy cases with G2D among children (<15 years)	1
Proportion of children (<15 years) among new leprosy cases (%)	28
Number of new leprosy cases among females	10
Proportion of females among new leprosy cases(%)	40

Figure 2. 14-year-old BaAka girl with MB leprosy. Manifestation of erytema nodosum leprosum on the limbs. Grade 2 Disability visible on the left hand; leprosy lesions on the ear lobe

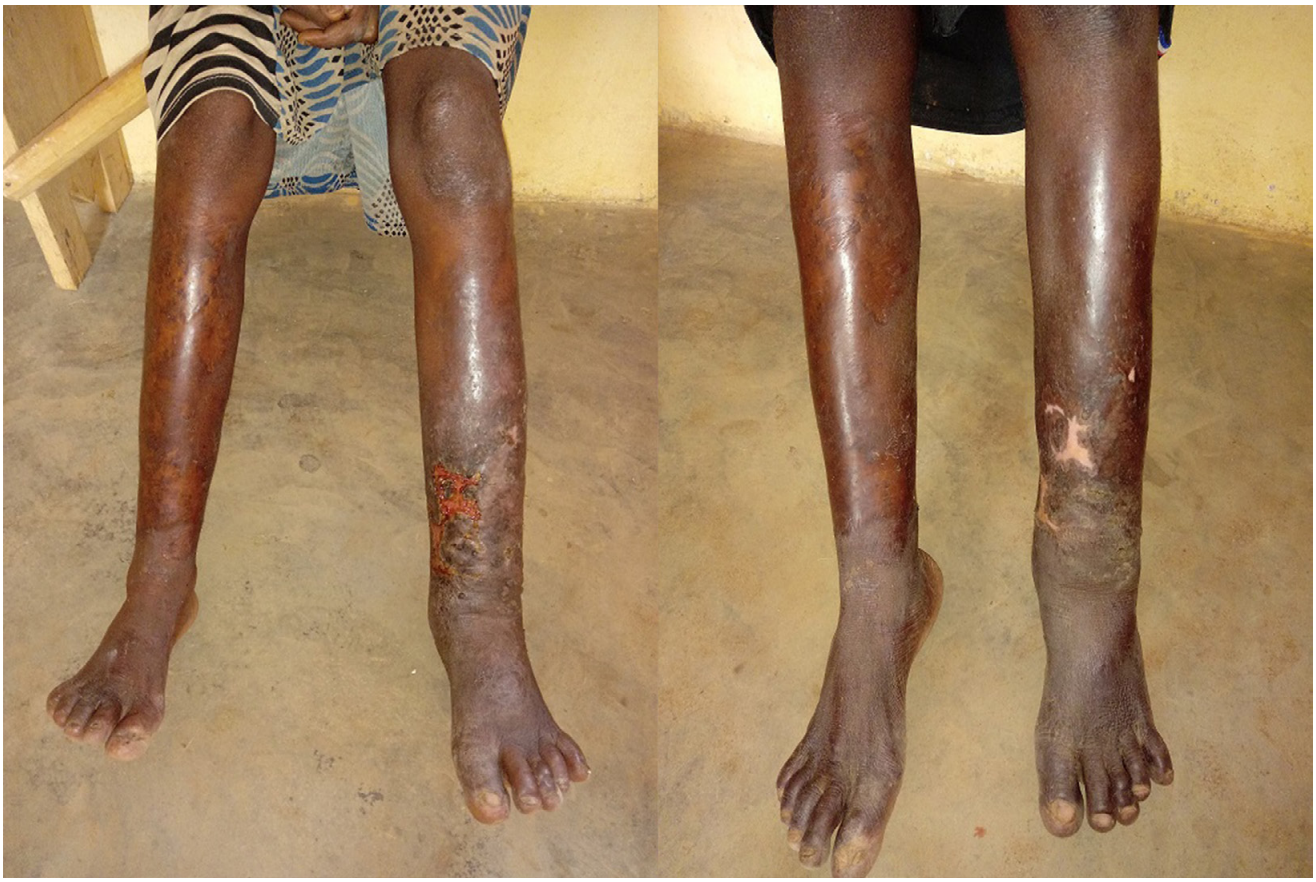

Figure 3. Evolution of leprosy manifestations on limbs after 2 and 3-month treatment with MDT (left and right photos, respectively) in the BaAka girl presented in Figure 2

DISCUSSION

Leprosy has been recognized as a neglected tropical disease [24]. Neglected diseases may affect as many as one billion people worldwide and are endemic in many parts of the world, especially in the tropics and sub-tropics [25]. The elimination of neglected diseases is difficult because they are closely interrelated with poverty and environmental conditions [25]. These two factors are responsible for the fact that the incidence of leprosy cases has remained constant in recent years, despite the efforts and substantial financial support of the WHO [1, 3]. There are about 200,000 leprosy cases detected each year, of which about 95% are registered in 23 countries recognized by WHO as a major target in

Figure 4. A 25-year-old BaAka leprosy patient before treatment for MB leprosy

Figure 5. The Patient from Figure 4 after a 2-month treatment with MDT

the fight against leprosy, however, the CAR is not one of them [12].

Despite the availability of MDT, which is fully effective and offered free of charge worldwide, initially by the Nippon Foundation from 1981 and since 2000 by the Novartis Foundation, [12, 26], access to these drugs in some countries, notably in the CAR, is limited by insufficient logistics and distribution networks, and the lack of data on new leprosy cases and the demand for drugs in areas such as Dzanga Sangha.

According to WHO data, the number of new leprosy cases registered in 2019 globally was 202,185 [12]. In 2011–2019, the number of new leprosy cases per one million people had been steadily decreasing globally, from 33.7 in 2011 to 26.5 in 2019, while the number of new leprosy cases in children decreased from 11.0 cases per one million children in 2011, to 7.6/1 million in 2019 and totalled 14,981, which accounted for 7.4% of all registered cases [27].

The data presented here show that the proportions are much higher for the Dzanga Sangha region: 1,276.421 new cases per one million in the general population, and 633.312 new cases per one million in the paediatric population. Also, the proportion of children among the new leprosy cases is higher in the Dzanga Sangha region, compared with the CAR and worldwide WHO statistics (Tab. 5). Globally, women accounted for 38.9% of the total new cases. In Africa, this percentage was lower and amounted to 29.8%. The Dzanga Sangha region, however, shows the opposite trend as the proportion of women among new cases is 40% [27] (Tab. 4). The data on new leprosy cases in the Dzanga Sangha area have been calculated according to the latest demographic statistics collected for the World Wild Fund for Nature (WWF) in 2021. The total population of the Dzanga Sangha area is 19,586, including 11,053 children.

Table 5. Number of leprosy cases in the Dzanga Sangha region compared with the 2019 WHO data on leprosy cases in the CAR

	Dzanga Sangha Mobile Clinic Data 2019	WHO data Central African Republic 2019
Number of new leprosy cases	**25**	**343**
New leprosy case detection rate per 1 000 000 population	**1276.421**	**72.284**
Number of leprosy cases registered for treatment	**24**	No data
Leprosy registered for treatment prevalence rate per 1 000 000 population	**1225.365**	No data
Number of new leprosy cases with G2D	**8**	No data
Proportion of new leprosy cases with G2D (%)	**32**	No data
New leprosy cases with G2D per 1 000 000 population	**408.455**	No data
Number of new leprosy cases among children (<15 years)	**7**	**57**
New leprosy child detection rate (<15 years) per 1 000 000 child population	**633.312**	**27.35**
Number of new leprosy cases with G2D among children (<15 years)	**1**	No data
Proportion of children (<15 years) among new leprosy cases(%)	**28**	**16.6**
Number of new leprosy cases among females	**10**	No data
Proportion of females among new leprosy cases(%)	**40**	No data

There had been no leprosy cases reported among BaAka Pygmies and no BaAka patients had been treated for leprosy in at least the past five years; therefore, it may be assumed that 100% of the registered cases among BaAka patients were new leprosy cases. The WHO data for 2020 came from 127 countries worldwide; however, the Central African Republic is not among them [12].

WHO's Global Leprosy Strategy for 2021–2030 aims at elimination of leprosy, defined as interruption of the disease transmission. In 2030, 120 countries are expected to report zero indigenous leprosy cases, a 70% annual reduction of new leprosy cases, a 90% reduction in the rate of new cases among children, and a 90% reduction in the rate of new G2D cases [12]. This is likely to be a great challenge for many countries like the CAR.

The data obtained from this study has been compared with the WHO official data for 2019 and 2020; the two sets of data show significant differences, which suggests lack of reporting to the district hospitals by health facilities located in the rural areas of the CAR (Tab. 4 and 5). The differences between the data may suggest that actual numbers of leprosy cases could be significantly higher than those presented in official reports. A significant reduction in leprosy prevalence in 2020, compared with 2019, may also be due to difficulties in reporting during the Covid-19 pandemic and should be interpreted with caution [12].

The CAR is one of the poorest countries in the world, with a *per capita* income of US $511.5 per year in 2021, making it the fourth poorest country in the world [28]. These economic data presented in World Bank statistics largely ignore the BaAka Pygmy community, which is not included in the official population statistics. Poverty, poor hygiene and, usually, a large number of people per household, facilitate the transmission of diseases spread through contact with infected individuals.

Children under the age of five years are protected by vaccine-preventable diseases by a vaccination schedule. However, due to their partially nomadic lifestyle and the lack of medical documentation, BaAka Pygmies usually only receive basic vaccinations according to the schedule, or do not receive them at all, e.g. the BCG (Bacille Calmette-Guerin) vaccination. There is evidence that BCG vaccination has a protective effect against leprosy by enhancing the cellular response to *M. leprae* antigens, and increasing the production of inflammatory mediators [29]. The presence of post-vaccination scar was not assessed in this study, thus it is not known how many leprosy-patients received the BCG vaccination.

The role of animals in the leprosy transmission chain, such as armadillos, red squirrels and apes, remains unclear [15, 30]. For the past two decades the number of new leprosy cases has stabilized at the level of 200,000 cases every year, despite the availability of effective treatment. One hypothesis suggests that the difficulties in leprosy eradication might be due to the existence of additional leprosy transmission routes, such as zoonotic transmission. MDT stops direct human to human transmission, but it has no effect on hypothetical zoonotic pathway[15]. In the Dzanga Sangha region, both armadillos and apes are present.

CONCLUSIONS

Despite many years of research, leprosy is still not fully understood. Active search for new cases is essential [12, 27] to accelerate rapid detection of all new leprosy cases, especially in vulnerable populations such as the BaAka Pygmy population of the CAR. The healthcare system and drug distribution networks, as well as treatment supervision, need to adjust to the nomadic lifestyle of BaAka patients in order to be effective, and to avoid the stage of disabling deformation and loss of distal parts of fingers and toes. Presented data show important differences between national data presented in WHO statistics and the presented group of 26 leprosy patients in the Dzanga Sangha region. Current research shows the high proportion of leprosy cases within children, which is the result of the high transmission rate in the area, a high proportion of new leprosy cases with grade 2 disability and a high proportion of leprosy cases within the female population. Presented data shows that the leprosy situation in Dzanga Sangha region is not well controlled and the efforts in fighting against leprosy should be intensified. The lack of data or inaccurate statistics erodes the fight against leprosy. Education about the sources, symptoms and transmission pathways of the disease within the native populations is essential to reach compliance.

In times of the mass migration taking place all around the world, it is necessary to share knowledge about this neglected disease because of the risk of spreading the disease from endemic areas to countries considered to be leprosy-free.

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