Silvana Margarida Benevides Ferreira[I,II]

Eliane Ignotti[III]

Ligia Maria Senigalia[IV]

Diego Ricardo Xavier Silva[V]

Mônica Antar Gamba[VI]

Recurrence of leprosy cases in the State of Mato Grosso, Central-West Brazil

ABSTRACT

OBJECTIVE: To compare new registrations of recurrences of leprosy cases in primary healthcare units (PHUs) and in specialized units in the State of Mato Grosso.

METHODS: This was a cross-sectional study based on all new registrations (N = 323) of recurrences of leprosy cases within the Notifiable Disease Information System (SINAN) between 2004 and 2006 that were made in the State of Mato Grosso, Central-West Brazil. The cases diagnosed were compared regarding sex, age, clinical-laboratory characteristics and geographical distribution among the municipalities. To compare and calculate the proportions of the variables, the chi-square test at the significance level of 5% was used.

RESULTS: Among the new registrations of recurrences, 20% were confirmed at specialized units and 80% at PHUs. However, most of the diagnoses at PHUs presented negative bacilloscopy findings (c2 = 12.34; p = 0.002). Seventy-one per cent of the cases were among males; the mean age was 43 years. No differences in the percentages of registrations were observed between the healthcare units with regard to clinical form, operational classification or degree of physical incapacity. Out of the total number of municipalities in the state, 64.7% presented recurrences and these accounted for 6 to 20% of all registrations.

CONCLUSIONS: The new registrations of cases of recurrence in Mato Grosso were influenced by the diagnoses made at PHUs, thus suggesting that there is a deficiency within the healthcare services in recognizing cases of recurrence.

DESCRIPTORS: Leprosy, epidemiology. Recurrence, prevention & control. Disease Notification. Cross-Sectional Studies.

INTRODUCTION

Leprosy control began at the end of the 1940s,[4] with the introduction of sulfones to treat the disease. After some time, given the inefficiency of this therapy, studies on resistance to sulfone monotherapy began.[8] The existence of this resistance was proven experimentally by Pettit & Rees in 1964,[15] by means of the technique of inoculation of *Mycobacterium leprae,* as standardized by Shepard.[17] From the 1980s onwards, the World Health Organization (WHO) started to recommend the use of polychemotherapy regimens. This has resulted in treatment and cure for more than 11 million leprosy patients.[a] Polychemotherapy has been decisive in shortening the duration of treatments, thereby leading to an inversion in the flow of cases coming into and leaving

[a] Organização Mundial da Saúde. A estratégia do esforço final para a eliminação da hanseníase: plano estratégico, 2000–2005. Geneva; 2000.

[I] Faculdade de Enfermagem. Universidade de Cuiabá. Cuiabá, MT, Brasil

[II] Secretaria Municipal de Saúde de Cuiabá. Cuiabá, MT, Brasil

[III] Departamento de Enfermagem. Universidade do Estado de Mato Grosso. Cáceres, MT, Brasil

[IV] Hospital Jardim Cuiabá. Cuiabá, MT, Brasil

[V] Instituto de Comunicação e Informação Científica e Tecnológica em Saúde. Fundação Oswaldo Cruz. Rio de Janeiro, RJ, Brasil

[VI] Escola Paulista de Enfermagem. Universidade Federal de São Paulo. São Paulo, SP, Brasil

Correspondence:
Silvana Margarida Benevides Ferreira
Universidade de Cuiabá – Unic
R. Av. Beira Rio, 3100 – Dom Aquino
78065-900 Cuiabá, MT, Brasil
E-mail: jffbenev@terra.com.br

Received: 10/26/2009
Approved: 12/18/2009

Article available from: www.scielo.br/rsp

the registers of active leprosy cases and a decline in the coefficient of prevalence in most endemic countries.[b]

However, after discharge from polychemotherapy, some leprosy cases may present intercurrences of the disease, either because of states of leprosy reaction or because of recurrences.[3,20,21,c]

Recurrences are the most important indicator of treatment effectiveness,[a] even if leprosy recurrences may be caused by strains that are monoresistant or multiresistant to chemotherapy.[4,7,12,13,15]

According to the Brazilian Ministry of Health,[d] the clinical criteria for diagnosing recurrence should be based on the operational classification, when the possibility of a reaction state has been ruled out. Paucibacillary patients are considered to be cases of recurrence when, after discharge because cure was achieved, they present impaired neural function, new areas with abnormal sensitivity, new lesions and/or exacerbation of previous lesions that do not respond to corticosteroid treatment within a 90-day period. For multibacillary patients, it is when they present the same dermatological-neurological abnormalities as described for paucibacillary patients, with the addition of results from bacilloscopic and/or histopathological examinations that are compatible with the active forms of the disease, and when they do not respond to treatment with corticosteroids and/or thalidomide. Confirmation of such recurrence should be discussed with specialists at reference centers, according to the criteria for diagnostic suspicion and confirmation.[c]

At the start of 2007, there were 2,270 cases of recurrence around the world, of which 1,584 (69.8%) were registered in Brazil.[b] According to the Brazilian Ministry of Health, the cumulative risk of recurrence after polychemotherapy was adopted was 0.7% for cases subjected to a multibacillary regimen and 1.1% for paucibacillary cases.[e]

Furthermore, there are important differences in the records of recurrence in Brazilian regions where there is high prevalence of the disease, such as the borders of the Statutory Amazon Region. The states of Mato Grosso, Acre, Amazonas, São Paulo, Paraná and Santa Catarina register the highest rates in Brazil: between 4% and 8% of the cases of recurrence among all the registrations in 2006.[f]

Studies that identify factors relating to recurrence are essential for better accuracy to be obtained in relation to the clinical, epidemiological and therapeutic diagnoses, thereby avoiding increased morbidity, persistence of bacteria, resistance to medications and physical incapacity. Through these high numbers of recorded cases of recurrence in Mato Grosso, the present study had the objective of comparing the records of leprosy cases diagnosed at primary healthcare units and specialized units in the state of Mato Grosso.

METHODS

This was a cross-sectional study using the registrations caused by leprosy recurrence that were notified in the state of Mato Grosso, Central-West Brazil, between 2004 and 2006. These were obtained from the notifiable diseases information system (SINAN/MT). The cases selected were patients living in the municipalities of Cuiabá, Cáceres, Diamantino, Rondonópolis or Várzea Grande, between 2004 and 2006. These municipalities were selected because they had diagnostic and leprosy study support units: polyclinics, medical specialty centers and the medium and high complexity reference center (CERMAC). These municipalities have 1,032,523 inhabitants, i.e. 36.2% of the total population of the state, which is estimated to be 2,854,462 inhabitants.[g] The comparative analysis included the cases diagnosed as recurrence at specialized units, the individuals living in the five municipalities selected and those diagnosed in primary healthcare units in the other municipalities of the state. The cases were compared with regard to sex, age, clinical-laboratory characteristics and geographical distribution among the municipalities of the state.

All registrations of recurrence (n = 344) were included according to the municipality of residence. From this total, 21 registrations were excluded because of diagnostic error, double data entries and transfers to other states, and thus 323 cases registered over the study period were evaluated. To validate the data relating to the three cases of double data entry, the treatment units were consulted. For this study, the diagnostic unit and its municipality were used. In selecting the cases of recurrence, the date and year of diagnosis were used. In most cases, these coincided with the date and year of treatment. When there was disagreement or failure to fill in the date and year field in the medical records, it was

[b] Weekly epidemiological record. Relevé épidémiologique hebdomadaire. Geneva: World Health Organization; 2007;25(82).
[c] Ministério da Saúde. Guia para o controle da hanseníase. Brasília; 2002. (Cadernos de Atenção Básica, 10).
[d] Ministério da Saúde. Portaria Conjunta nº 125, de 26 de março de 2009. Define ações de controle da hanseníase. *Diario Oficial União*. 27 mar 2009;Seção1:73.
[e] Ministério da Saúde. Secretaria de Políticas de Saúde. Departamento de Atenção Básica. Área Técnica de Dermatologia Sanitária. Hanseníase: atividades de controle e manual de procedimentos. Brasília; 2001.
[f] Ministério da Saúde. Departamento de Informática do Sistema Único de Saúde. Acompanhamento de hanseníase. Brasília; 2006 [cited 2008 Apr 04]. Available from: http://dtr2004.saude.gov.br/sinanweb/
[g] Instituto Brasileiro de Geografia e Estatística. Contagem da população 2007. População recenseada e estimada, segundo os municípios de Mato Grosso 2007. Rio de Janeiro, 2007.

sought to validate the data by means of the annotations in the medical files. The cases were classified according to the operational classification (paucibacillary or multibacillary), which was obtained through confirmation of the diagnosis of recurrence that was made at the diagnostic unit. No registrations of recurrence that presented changes in operational classification after the start of the retreatment were observed.

The following variables were selected for analysis: sex, age, municipality of residence, clinical form, operational classification, degree of physical incapacity evaluated at the start of the treatment and bacilloscopy at the time of diagnosing the recurrence.

The indicator of the percentage of leprosy recurrence corresponded to the percentage of registrations of recurrence. This was defined as the number of recurrences during the years investigated, divided by all the registrations for leprosy treatment during the same year, multiplied by 100. For the denominator, the registrations with diagnostic error, double data entries and transfers to other states were also removed. The percentage recurrence was calculated for all the municipalities, taking into consideration the operational classification of the set of registrations for each locality.

The municipalities were aggregated according to the type of healthcare unit, in order to compare the clinical-laboratory criteria used in the units for diagnosing the recurrence.

To compare the total numbers of cases of recurrence between the primary healthcare units (PHU) and the specialized units (SU), according to the operational classification, the ratio of the percentages of cases of recurrence [(PHU/SU)-1)*100] was calculated using an electronic spreadsheet.

To compare and calculate the proportions according to the relative frequencies of the variables, the chi-square test was used in Epi-Info, version 3.2.1. The geographical distribution of the records of percentage recurrence was performed by means of the Terraview software, version 3.2.0.

The present project was evaluated and approved by the Research Ethics Committee of the Hospital Universitário Júlio Muller (CEP/HUJM – procedural number 321), in April 2007.

Table 1. Comparison of the percentages of leprosy registrations due to recurrence, diagnosed at primary healthcare units and specialized units, according to selected variables. State of Mato Grosso, Central-West Brazil, 2004-2006.

Variable	Recurrence				Total		χ^2 (p value)
	Primary healthcare unit		Specialized unit				
	n	%	n	%	n	%	
Sex							
Male	180	69.8	49	75.4	229	70.9	0.79 (0.373)
Female	78	30.2	16	24.6	94	29.1	
Age (years)							
≥ 15	253	98.1	65	100.0	318	98.5	
Clinical form							
Indeterminate	26	10.1	03	4.6	29	9.0	5.22 (0.266)
Tuberculous	21	8.1	07	10.8	28	8.7	
Dimorphous	125	48.4	31	47.7	156	48.3	
Virchow	41	16.0	16	24.6	57	17.6	
Unknown	45	17.4	08	12.3	53	16.4	
Operational classification							
Paucibacillary	46	17.8	11	16.9	57	17.6	0.03 (0.864)
Multibacillary	212	82.2	54	83.1	266	82.4	
Degree of physical incapacity at diagnosis							
Zero	141	54.6	41	63.1	182	56.3	4.44 (0.218)
G1	59	22.9	17	26.1	76	23.5	
G2 and G3	18	7.0	02	3.1	20	6.2	
Unknown	40	15.5	05	7.7	45	14.0	
Total[a]	258	79.9	65	20.1	323	100.0	

Source: Notifiable Diseases Information System (SINAN/leprosy). State Health Department of Mato Grosso (SES/MT), 2004-2006.

[a] percentage calculated on the line

RESULTS

The 323 cases of recurrence of leprosy registered in Mato Grosso between 2004 and 2006 represented a mean of 107.6 cases/year.

Table 1 presents a comparison of percentages of registrations due to recurrence that were diagnosed in the primary healthcare units and specialized units, according to the variables of sex, age, clinical form, operational classification and degree of physical incapacity at diagnosis. No statistically significant difference in percentages was seen between the healthcare units according to sex. The majority (71%, n = 229) of the patients with recurrence were male; the mean age was 42.6 years (SD = 15.8; minimum 12 years and maximum 84 years). The five children with recurrence were diagnosed in primary healthcare units. The municipality of Cuiabá presented the highest percentage (13%; n = 43). Out of all the records of recurrence, 20.1% were diagnosed in specialized units and 79.9% in primary healthcare units. In general, the dimorphous form accounted for 48% (n = 156) of the registrations; 82% (n = 266) were multibacillary and 56% (n = 182) did not have any physical incapacity. There were no differences in the percentages of registrations between the units according to the clinical form, operational classification or degree of physical incapacity.

There was a statistically significant difference in the percentage of cases of recurrence between the diagnostic units, according to the bacilloscopy results [χ^2 = 5.86 (p = 0.053)] (Table 2). Among the cases of multibacillary recurrence, 37% (n = 76) were diagnosed with a negative bacilloscopy result in primary healthcare units [χ^2 = 12.34 (p = 0.002)].

In Table 3, it can be seen that the difference in the percentages of diagnoses of recurrence among all the registrations for leprosy treatment, between those at primary healthcare units and those at specialized units was 116%. For the category of cases of paucibacillary recurrence, this difference reached 150%.

The Figure presents the geographical distribution of registrations of cases of leprosy recurrence according to municipality of residence, in the categories of total number of cases of recurrence (A), cases of multibacillary recurrence (B) and cases of paucibacillary recurrence (C). Out of the 141 municipalities in Mato Grosso, 139 presented notifications of leprosy cases. Among this total, 64.7% (n = 90) registered cases of recurrence, among which 14% (n = 13) presented more than five cases, with percentages of 6% to 20% of all the registrations. Multibacillary cases accounted for most of the registrations and there was no difference in this respect between geographical areas of the state. Total of more than five paucibacillary cases were registered in the municipalities of Cuiabá and Araputanga.

DISCUSSION

The results obtained showed that a larger percentage of the registrations of recurrence were diagnosed at primary healthcare units. Most of these cases were confirmed, even if the bacilloscopy results were negative. Such results suggest that there were deficiencies relating to operational factors, including the capacity of the healthcare service network to diagnose cases of recurrence.

Table 2. Comparison of the percentages of leprosy registrations due to recurrence, diagnosed at primary healthcare units and specialized units, according to the bacilloscopy result for the diagnosis and operational classification. State of Mato Grosso, Central-West Brazil, 2004-2006.

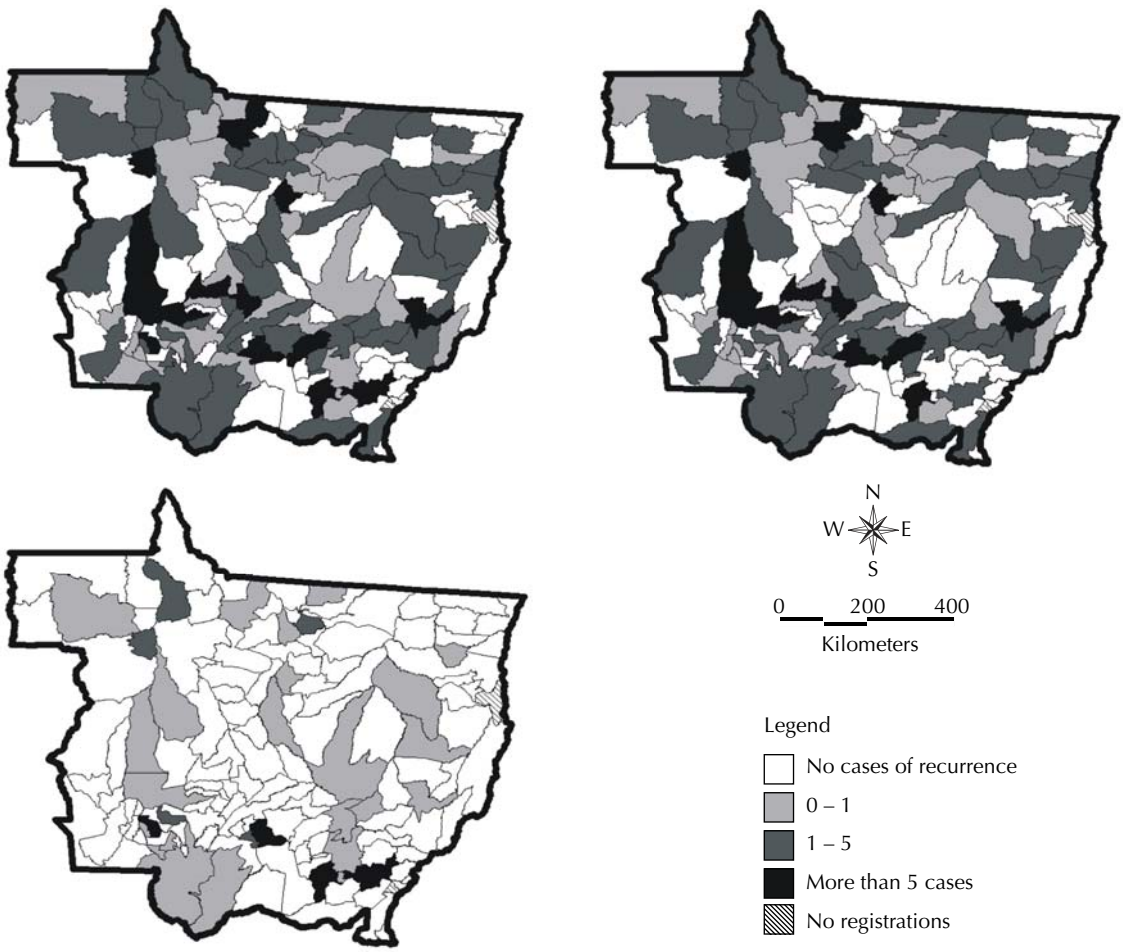
Variable	Recurrence				Total		χ^2 (p value)
	Primary healthcare unit		Specialized unit				
	n	%	n	%	n	%	
Bacilloscopy							
Positive	67	26.0	22	33.8	89	27.6	
Negative	101	39.1	15	23.1	116	35.9	5.86 (0.053)
Not recorded/unknown	90	34.9	28	43.1	118	36.5	
Bacilloscopy (paucibacillary)							
Positive	01	2.5	02	11.7	03	5.3	
Negative	22	55.0	07	41.2	29	50.9	2.45 (0.294)
Not recorded/unknown	17	42.5	08	47.1	25	43.8	
Bacilloscopy (multibacillary)							
Positive	68	33.2	18	29.5	86	32.3	
Negative	76	37.1	11	18.0	87	32.7	12.34 (0.002)
Not recorded/unknown	61	29.7	32	52.5	93	35.0	

Source: Notifiable Diseases Information System (SINAN/leprosy). State Health Department of Mato Grosso (SES/MT), 2004-2006

Table 3. Ratio of percentages of recurrence of leprosy in primary healthcare units and specialized units, according to operational classification. State of Mato Grosso, Central-West Brazil, 2004-2006.

Variable	Primary healthcare unit			Specialized unit			Total			Difference % recurrence
	Total number of cases	Recurrence (A)		Total number of cases	Recurrence (B)		Total number of cases	Recurrence		
	n	n	%	n	n	%	n	n	%	
Paucibacillary	9,959	46	0.5	6,116	11	0.2	16,075	57	0.4	150.0
Multibacillary	10,338	212	2.1	4,723	54	1.1	15,061	266	1.8	90.9
Total	20,297	258	1.3	10,839	65	0.6	31,136	323	1.0	116.7

Source: Notifiable Diseases Information System (SINAN/leprosy). State Health Department of Mato Grosso (SES/MT), 2004-2006.



Source: Notifiable Diseases Information System (SINAN/leprosy). State Health Department of Mato Grosso (SES/MT), 2004-2006.

Figure. Geographical distribution of registrations of leprosy cases in the municipalities of residence, according to (A) total number of cases of recurrence, (B) cases of multibacillary recurrence and (C) cases of paucibacillary recurrence. State of Mato Grosso, Central-West Brazil, 2004-2006.

According to the Brazilian Ministry of Health (2006),[h] the criteria for certifying healthcare units as reference centers for leprosy include: a multidisciplinary team with up-to-date training for healthcare relating to leprosy; provision of healthcare at specialized level, to clarify diagnoses, recurrences and intercurrences relating to episodes of reaction and neural lesions of leprosy, among others.

[h] Ministério da Saúde. Secretaria de Vigilância em Saúde. Portaria SVS/MS nº 11, de 2 de março de 2006. Define critérios para habilitação de unidades de saúde como centro de referência de hanseníase. *Diario Oficial Uniao.* 3 mar 2006;Seção1:48.

The patients diagnosed in Mato Grosso presented epidemiological characteristics similar to those of patients undergoing treatment in Brazilian cities in other states.[2] The cases were predominantly among males, at economically productive ages, and in the multibacillary form.

Occurrences of cases among children are an important epidemiological indicator, and analysis of such cases broadens the discussion regarding operational problems within the healthcare network.[1,10] The records of cases of recurrence at primary healthcare units among the present study population corroborate this reflection, because of difficulty in differential approaches in relation to other dermatological or neurological diseases and difficulty in diagnostic management for confirming the case of recurrence.

The importance of these results justifies the recommendation to follow a protocol for diagnostic actions and follow-up of cases of recurrence in specialized units, with implementation of laboratory support and quality control on the specific tests.[3,c]

Through the introduction of the basic operational standards (1996),[i] it was envisaged that patients' access to basic and specialized healthcare services would be improved. In Mato Grosso, specialized attendance for leprosy is concentrated in municipalities with medium and large-sized populations (Cuiabá, Cáceres, Rondonópolis and Várzea Grande). In the remaining municipalities in this state, access to diagnoses of greater accuracy for cases of recurrences is more difficult.

Among other factors, the weaknesses of primary healthcare units in terms of case resolution have been indicated as one of the problems for maintaining the strategy of changes to the care model,[5] especially regarding the hierarchical flow for attendance. The lack of mechanisms for regulating the municipalities' responsibilities may explain the deficiency in the quality of care.[14] Other studies[16,19] have indicated that there are higher percentages of recurrence among paucibacillary patients than among multibacillary patients, thus differing from the percentages found in this study (greater percentages for recurrence in the multibacillary cases). These results may suggest that healthcare professionals find it easier to confirm the diagnosis in multibacillary cases. Among the clinical forms, recurrences in multibacillary cases are mostly confirmed through a bacilloscopic index ≥ 2 logs, in relation to the initial treatment, through histopathological examinations compatible with active forms of the disease, and through inoculation in a mouse's paw.[17-19,21] Although bacilloscopic index results were not analyzed in the present study, given that this indicator was not available within SINAN during the study period, the higher percentage of negative bacilloscopy results obtained at primary healthcare units also suggests that there is a greater likelihood of diagnostic errors in distinguishing between reactional states and recurrence.

Reactional states or leprosy reactions are reactions of the patient's immune system to *M. leprae*. The clinical signs, which are called inflammatory episodes, may affect both paucibacillary and multibacillary cases, and when they appear following chemotherapy, they may be confounded with cases of recurrence.[3,9,11,20]

According to Ximenes et al (2007)[21] and Shetty et al (2005),[18] patients who present reactional episodes are more likely to be treated as cases of recurrence. This indicates that there is a need for greater attention to the differential diagnosis between these two conditions. Among paucibacillary patients, recurrence can be confounded with a late reverse reaction, considering that *M. leprae* cannot be isolated in these cases.[9]

According to Gallo & Oliveira,[9] in addition to the difficulty of characterizing patients with recurrence, there is no consensus regarding established parameters that might guide healthcare services towards diagnostic confirmation. There is therefore a need to conduct studies that might direct healthcare professionals towards such confirmation, with greater precision.

The paucibacillary cases registered as recurrences in municipalities with populations of fewer than 20,000 inhabitants (Araputanga, Castanheira, Guiratinga, Nova Bandeirantes, Salto do Céu and Terra Nova do Norte) stood out. These municipalities had lower capacity for diagnosing cases of recurrence and did not have reference centers to ensure the accuracy of diagnoses.

The Brazilian National Health System (SUS)[j] recommends that municipalities should organize primary healthcare service, while the State should impose standards, perform assessments, provide technical advice and reorganize the referral and counter-referral system.

Within this context, effective attendance for leprosy depends on improvement of the leprosy indicators agreed at managerial levels within SUS.[k]

This study presents the limitations inherent to cross-sectional studies conducted using secondary data. It is known that healthcare professionals who are well-qualified in diagnosing and treating leprosy, with professional experience obtained because of the high prevalence of

[i] Ministério da Saúde. NOB – SUS 1996. Norma Operacional Básica do Sistema de Saúde: Gestão plena com responsabilidade pelo cidadão. Brasília; 1997.

[j] Brasil. Portaria nº 95, de 26 de janeiro de 2001. Norma operacional da assistência à saúde. NOAS-SUS 01/2001. *Diario Oficial Uniao.* 29 jan 2006;Seção1:48.

[k] Ministério da Saúde. Aplicativo do pacto pela saúde (SISPACTO). Available from: http://portalweb04.saude.gov.br/sispacto/

this disease, may be allocated to primary healthcare units in Mato Grosso, away from the state capital.[6] However, the technological difficulties in meeting the diagnostic criteria for recurrence of leprosy at these units reduces the importance of the points made above regarding the limitations of the study, to some extent.

It is concluded that the numbers of new cases of recurrence registered in Mato Grosso are influenced by the diagnoses made in primary healthcare centers, thus suggesting that there are deficiencies within the healthcare services, with regard to recognizing cases of recurrence.

REFERENCES

1. Alencar CHM, Barbosa JC, Ramos Jr NA, Alencar MJF, Pontes RJS, Castro GJC, et al. Hanseníase no município de Fortaleza, CE, Brasil: aspectos epidemiológicos e operacionais em menores de 15 anos (1995-2006). *Rev Bras Enferm*. 2008;61(Esp):694-700.
2. Aquino DMC, Caldas AJM, Silva AAM, Costa JML. Perfil dos pacientes com hanseníase em área hiperendêmica da Amazônia do Maranhão, Brasil. *Rev Soc Bras Med Trop*. 2003;36(1):57-64. DOI:10.1590/S0037-86822003000100009
3. Azulay RD, Azulay DR, Azulay-Abulafia L. Dermatologia. 5. ed. Rio de Janeiro: Guanabara Koogan; 2008.
4. Baohong J. Drug resistance in leprosy: a review. *Leprosy*. 1985;56(4):265-78.
5. Canesqui AM, Spinelli MAS. Saúde da Família no Estado de Mato Grosso, Brasil: perfis e julgamentos de médicos e enfermeiros. *Cad Saude Publica*. 2006;22(9):1881-92. DOI:10.1590/S0102-311X2006000900019
6. Cortela DCB, Ignotti E. Lesões na hanseníase: o papel do cirurgião-dentista na suspeita de casos novos. *Rev Bras Epidemiol*. 2008;11(4):619-32. DOI:10.1590/S1415-790X2008000400010
7. Drug resistance in leprosy: reports from selected endemic countries. *Weekly Epidemiological Record*. 2009,26(84):261-268.
8. Floch H. La sulfono-résistance du bacille de Hansen. *Arch Inst Pasteur Guyane Franc Terit Inini*. 1957;429:1-9.
9. Gallo MEN, Oliveira MLW. Recidivas e reinfecção em hanseníase. *Medicina (Ribeirão Preto)*. 1997;30(3):351-7.
10. Imbiriba EB, Hurtado-Guerrero JC, Garnelo J, Levino A, Cunha MG , Pedrosa V. Perfil epidemiológico da hanseníase em menores de quinze anos de idade, Manaus (AM), 1998-2005. *Rev Saude Publica*. 2008;42(6):1021-6. DOI:10.1590/S0034-89102008005000056
11. Linder K, Zia M, Kern WV, Pfau RKM, Wagner D. Relapses vs. reactions in multibacillary leprosy: proposal of new relapse criteria. *Trop Med Int Health*. 2008;13(3):295-309.
12. Maeda S, Matsuoka M, Nakata N, Kai M, Maeda Y, Hashimoto K, et al. Multidrug resistant Mycobacterium leprae from patients with leprosy. *Antimicrob Agents Chemother*. 2001;45(12):3635-9. DOI:10.1128/AAC.45.12.3635-3639.2001
13. Matsuoka M, Budiawan T, Aye KS, Kyaw K, Tan EV, Cruz ED, et al. The frequency of drug resistance mutations in Mycobacterium leprae isolates in untreated and relapsed leprosy patients from Myanmar, Indonesia and the Philippines. *Lepr Rev*. 2007;78(4):343-52.
14. Melo AM. A política da ação regulatória: responsabilização, credibilidade e delegação. *Rev Bras Ci Soc*. 2001;16(46):1-16. DOI:10.1590/S0102-69092001000200003
15. Pettit JH, Rees RJ. Sulphone resistance in leprosy. An experimental and clinical study. *Lancet*. 1964;2(7361):673-4. DOI:10.1016/S0140-6736(64)92482-1
16. Samad AK. An analysis of relapsed leprosy cases. *Indian J Dermatol Venereol Lepr*. 2000;66(3):126-8.
17. Shepard CC. The experimental disease that follows the injection of human leprosy into food pads of mice. *J Exp Med*. 1960;112(3):445-54. DOI:10.1084/jem.112.3.445
18. Shetty VP, Wakade AV, Ghate SD, Pai VV, Ganapati RR, Antia NH. Clinical, histopathological and bacteriological study of 52 referral MB cases relapsing after MDT. *Lepr Rev*. 2005;76(3):241-52.
19. Suite M. Relapse rates following leprosy multidrug therapy. *West Indian Med J*. 2000;49(3): 210-1.
20. Walters MFR. Distinquishing between relapse and late reversal reaction in multidrug (MDT) – trated BT leprosy. *Lepr Rev*. 2001;72(3):337-44.
21. Ximenes RAA, Gallo MEN, Brito MFM. Retreatment in Leprosy: a case-control study. *Rev Saude Publica*. 2007;41(4):632-7. DOI:10.1590/S0034-89102006005000037

Study funded by the Research Support Foundation of the State of Mato Grosso (Fapemat; procedural number: PPSUS/275-10036).
Presented at the 11th Brazilian Congress of Leprosy Studies, in Porto Alegre, Southern Brazil, 2008.
The authors declare that there are not conflicts of interest.