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Risk factors for leprosy identified from cases notified in a period of 15 years

Factores de riesgo de lepra identificados en casos notificados en un periodo de 15 años

Fatores de risco para hanseníase identificados a partir de casos notificados num período de 15 anos

ABSTRACT
Objective: To identify and analyze risk factors for leprosy transmission over a 15-year period. Methods: Quantitative study, historical and observational. Data extracted from the SINAN. Statistical analyzes were the Mann-Whitney U method and spearman correlation in addition to univariate analyzes. Results: During the period, 514 cases were reported, In the univariate analysis model, men arrive at the service to be diagnosed with a greater number of injuries (p-value <0.05), with the clinical forms dimorphic and virchovian, (p-value <0.05) and with Degree of disabilities 1 and 2 (p-value <0.05). In the final model of multivariate analysis performed by means of logistic regression, significance was found for the association between the presence of physical disabilities and being diagnosed with multibacillaries, being over 52 years old and more than 3 injuries at the time of diagnosis. Conclusion: Sex and age have a higher risk of infection with leprosy. Socio-demographic risk factors did not show significance in the clinical variables.
DESCRIPTORS: Risk factors; Social Determinants of Health; Hansen's disease; Epidemiology.

RESUMEN
Objetivo: Identificar y analizar los factores de riesgo de transmisión de la lepra durante un período de 15 años. Métodos: Estudio cuantitativo, histórico y observacional. Datos extraídos del SINAN. Los análisis estadísticos fueron el método U de Mann-Whitney y la correlación de Spearman, además de los análisis univariados. Resultados: Durante el período se notificaron 514 casos. En el análisis univariante, los hombres llegan al servicio para ser diagnosticados con un mayor número de lesiones (valor p <0,05), con las formas clínicas dimórficas y virchowianas, (valor p <0,05) y con Grado de discapacidad 1 y 2 (valor de p <0,05). En el modelo final de análisis multivariado realizado mediante regresión logística, se encontró significancia para la asociación entre la presencia de discapacidad física y forma clínica multibacilar, edad mayor de 52 años y más de 3 lesiones en el momento del diagnóstico. Conclusión: el sexo y la edad tienen un mayor riesgo de infección por lepra. Los factores de riesgo sociodemográficos no mostraron significación en las variables clínicas.
DESCRIPTORES: Factores de Riesgo, Determinantes Sociales de la Salud, Lepra, Epidemiología.

RESUMO
Objetivo: Identificar e analisar os fatores de risco à transmissão da hanseníase num período de 15 anos. Métodos: Estudo quantitativo, observacional, de corte histórica, histórica e observacional. Dados extraídos do SINAN. As análises estatísticas foram método de U de Mann-Whitney e correlação de spearman, além de análises univariadas. Resultados: No período foram notificados 514 casos. Na análise univariada, os homens chegam ao serviço para serem diagnosticados com maior número de lesões (valor-p<0,05), com as formas clínicas dimorfa e virchowiana, (valor-p<0,05) e com Grau de incapacidades 1 e 2 (valor-p<0,05). No modelo final de análise multivariada realizada por meio de regressão logística, encontrou-se significância para associação entre presença de deficiências físicas e forma clínica multibacilar, idade maior de 52 anos e mais de 3 lesões no momento do diagnóstico. Conclusão: O sexo e a idade possuem maior risco de infecção à hanseníase. Fatores de riscos sociodemográficos não demonstraram significância nas variáveis clínicas.
DESCRITORES: Fatores de risco; Determinantes Sociais da Saúde; Hanseníase; Epidemiologia.

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INTRODUCTION

Leprosy remains a public health problem caused by Mycobacterium leprae, which is highly infectious and low pathogenic, which affects the peripheral nervous system and the integument, with a variety of signs of symptoms according to the clinical forms and poles having as one of the main characteristics is the changes in thermal, painful and tactile sensitivity. The patients' upper airways, especially untreated multibacillaries, are the elimination port that is also the most likely port of entry. It is a disabling disease, resulting in physical deficiencies especially in the eyes, hands and feet. It is one of the compulsory notification diseases according to Ministerial Decree No. 1.61 of May 18th, 2020, due to the impact on public health. The treatment is unique from September 2020 with the use of three drugs: Rifampicin, Dapsone and Clofazimine being 6 months for paucibacillaries and 12 months for multibacillaries according to Technical Note No. 4 of September 2020. [1-5]

The World Health Organization (WHO) has proposed the elimination of leprosy as a public health problem by the year 2020, that is, diagnosing less than 1 case for every 10,000 inhabitants and without apparent deformities. [6] In the world until 2016, 214.783 new cases of individuals affected by leprosy were reported, with a prevalence of 2.9/100.000, in the Americas there was an increase of 14% referring to 2015, and Brazil stood out in first place on the continent, occupying the 2nd place in the world, with 13% of new cases (26.395) with a detection rate of 12.2/100,000 inhabitants. [6,7]

In the State of São Paulo there is a gradual decrease in the prevalence coefficient from 1985 to 2015, standing at 0,38/10,000 inhabitants, with a decrease in the rate of detection of new cases from 2001 to 2017, until then 2,03% (3,8). The municipality of São José de Rio Preto (SJRP) has maintained the goal of eliminating the disease since 2007, when it reached less than one case per 10.000 inhabitants, but there are important fluctuations, in 2007 it had a prevalence of 0,99 cases/10.000 inhabitants, in 2009 it reached the lowest parameter and presented 0.33/10,000 inhabitants, but the prevalence increased year by year and in 2018 it reached 0.80/10.000 inhabitants. [9,10]

When analyzing the behavior of a disease, we inevitably analyze the risk factors and the literature shows that living and working conditions are related to the different levels of health experienced by people, depending on the social position they occupy in society. [11] Among the existing models, we highlight the model by Dahlgren and Whitehead, factors such as sex, age, lifestyle, living and working conditions, among others, are observed, which allows us to visualize the existing relationships with different levels of health. [12]

The observation of the emergence of diseases related to other factors, not only biological ones, leads to the reflection on why certain populations are more subject to illness and are more vulnerable to certain diseases. [13] This inequality in socially generated health levels, which could be avoided by means of appropriate public policies, is called health inequities. [11] Monteiro et al.[14] report that the "municipalities are fundamental units in the study of the social reproduction of the disease in which the cultural and economic relations of the groups in their collectivity materialize" and that the analysis of the data in "different spatial contexts is fundamental to qualify the different specificities and vulnerabilities ".

In this sense, the work aims to identify and analyze the risk factors for leprosy transmission in a city in the interior of the State of São Paulo. It is considered important to know them to contribute to the municipality in the (re) planning of the actions of this Program so that the goal of elimination can be reached according to the one proposed by the World Health Organization. [6]

METHOD

The design of this study is of an observational, descriptive, cross-sectional, retrospective, historical and quantitative cut, which used secondary data, of leprosy cases, notified in the Notifiable Diseases Information System (Sistema de Informação de Agravos de Notificação - SINAN), in the period of 15 (2001 to 2016) in the municipality of São José do Rio Preto.

The municipality is located in the interior of the State of São Paulo, 442 km from the capital, with an estimated population of 456.245 thousand inhabitants in 2018, with a total area of 431,963 km and a demographic density of 945,12 inhab./ Km2. This municipality is considered an important reference for the region and the surrounding states of Minas Gerais and Mato Grosso do Sul, with easy access, as it is cut by railway lines, state and federal highways and has a regional airport.

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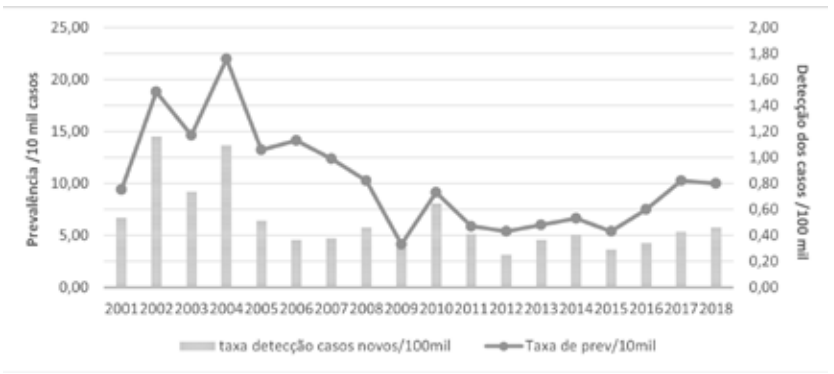
The municipality has an income distribution equal to 0,5081, which represents an unequal income distribution, and a human development index of 0,797, with a Firjan index of municipal development of 0,8753. The rate of adequate sanitary sewage coverage is 99%. [15-17]

The population of this study refers to leprosy cases (International Statistical Classification - ICD 10 from A30.0 to A30.9), which were diagnosed during the study period. The data were collected, from March to April 2018, through the bigdata, the Hansen Project of the Medical School of São José do Rio Preto (FAMERP), in agreement with the National Council for Scientific and Technological Development, and SINAN, made available online by the São Paulo State Department of Health. [8,10].

Due to the nature of this study, there was no need to submit it to Plataforma Brasil for consideration by the Ethics Committee, with approval for the use of secondary data by FAMERP.

The variables analyzed were clinical and epidemiological: year and date of notification, date of diagnosis, number of lesions, number of affected nerves, clinical form of the disease, number of evaluations performed, class of operation, mode of entry and mode of

Figure 1: Monitoring indicators of the progress of leprosy elimination in São José do Rio Preto, SP, Brazil, from 2001 to 2018. MS parameters prevalence per 10.000 inhabitants: hyper endemic: ≥20,0; very high: 10,0 to 19,9; high: 5,0 to 9,9; medium: 1,0 to 4,9 and low: <1,0. Parameters of the MS detection rate per 100.000 inhabitants: hyper endemic:>40,0, very high: 20,00 to 39,99; high: 10,00 to 19,99; medium: 2,00 to 9,99; low:<2,00.



Source: Brazil (3)

Figure 2: Association between clinical characteristics and gender of leprosy cases reported in São José do Rio Preto/SP, Brazil, from 2001 to 2016.

Características Clínicas	Sexo					
	Feminino		Masculino		TOTAL	
Lesões - p = (0,000)	**N**	**%**	**N**	**%**	**N**	**%**
Sem Lesão	74	33,64	84	28,57	158	30,74
Até 2 Lesões	70	31,82	54	18,37	124	24,12
> 2 Lesões	76	34,55	156	53,06	232	45,14
TOTAL	**220**	**100,00**	**294**	**100,00**	**514**	**100,00**
Nervos Afetados - p = (0,161)	**N**	**%**	**N**	**%**	**N**	**%**
Sem Nervos Afetados	66	30,00	92	31,29	158	30,74
Até 2 Nervos Afetados	19	8,64	35	11,90	54	10,51
> 2 Nervos Afetados	10	4,55	26	8,84	36	7,00
Missing	125	56,82	141	47,96	266	51,75
TOTAL	**220**	**100,00**	**294**	**100,00**	**514**	**100,00**
Forma Clínica - p = (0,000)	**N**	**%**	**N**	**%**	**N**	**%**
Indeterminado	46	20,91	23	7,82	69	13,42
Tuberculoide	61	27,73	35	11,90	96	18,68
Dimorfo	82	37,27	144	48,98	226	43,97
Vishoviano	31	14,09	92	31,29	123	23,93
TOTAL	**220**	**100,00**	**294**	**100,00**	**514**	**100,00**
Grau de incapacidades OMS - p = (0,002)	**N**	**%**	**N**	**%**	**N**	**%**
Grau 0	137	62,27	144	48,98	281	54,67
Grau 1	58	26,36	99	33,67	157	30,54
Grau 2	19	8,64	30	10,20	49	9,53
Não Avaliado	6	2,73	20	6,80	26	5,06
Missing	0	0,00	1	0,34	1	0,19
TOTAL	**220**	**100,00**	**294**	**100,00**	**514**	**100,00**
Classe Operacional - p = (0,000)	**N**	**%**	**N**	**%**	**N**	**%**
PB	107	48,64	58	19,73	165	32,10
MB	113	51,36	236	80,27	349	67,90
TOTAL	**220**	**100,00**	**294**	**100,00**	**514**	**100,00**
Modo de Entrada - p = (0,443)	**N**	**%**	**N**	**%**	**N**	**%**
Caso Novo	192	87,27	250	85,03	442	85,99
Transferência mesmo município	0	0,00	2	0,68	2	0,39
Transferência de outro município	7	3,18	10	3,40	17	3,31
Transferência de outro Estado	8	3,64	8	2,72	16	3,11
Recidiva	9	3,64	11	3,74	19	3,70
Outros reingressos	5	2,27	13	4,42	18	3,50
TOTAL	**220**	**100,00**	**294**	**100,00**	**514**	**100,00**

Source: Notifiable Diseases Information System (SINAN).

detection. And the variables of social determinants: age, sex, pregnancy, race, education, place of residence.

In the data analysis, Descriptive Statistics and inferential methods were used, evaluating probability questions of a population based on the sample data for better understanding, the following methods were used, mean, median, mode, standard deviation, standard error, maximum value and minimum, significance, and Poisson regression.

Hypothesis tests were performed, using the Mann-Whitney U method and the Spearman correlation, in which the behavior of the correlations between the analyzed variables and the degree of explanation of the dependent variable in relation to the independent variables of the sample were analyzed, in addition to univariate analyzes.

RESULTS

The WHO and the Ministry of Health use two important indicators to assess the magnitude and trend of the disease, namely: the prevalence rate, calculated on the number of cases undergoing treatment (active registration) in a given location until the last day of each year of assessment, divided by the total population at the same treatment site and year of assessment multiplied by 10.000. [2,6] And the annual detection rate of new leprosy cases that is calculated with new cases residing in a given location and diagnosed in the year of assessment (new cases), divided by the total resident population, in the same place and period, multiplied by 100 thousand inhabitants. [2]

In the figure below, it can be seen that, in the municipality and period studied, the prevalence with a peak of 1,76/10.000 inhabitants in 2004 and the detection with a significant increase in 2002, and both indicators with fluctuations.

From 2001 to 2016, 514 leprosy notifications were registered in SINAN,

with an average of 32,1 cases/year. In 2004, there was a peak of diagnosis, with 63 cases (12,26%), a higher incidence among men (57,2%), with the predominant age group of 15 - 59 years (70,8%) of white color (71<6%) with low education, living in the urban area of the municipality (88%).

As for the epidemic clinical data from 2001 to 2016, the predominance was for multibacillary (MB) (67,9%), dimorphic (44%) cases with less than or equal to five lesions on the body (35,8%). The assessments of the degree of physical disability in the diagnosis showed a higher incidence of Grade 0 (54,7%), which represents the absence of physical disability. Regarding the mode of entry, there were 442 (86%) of new cases, 19 (3,7%) of recurrent cases, 18 (3,5%) of other reentry; the other cases (35) came from other municipalities, states or transfers within the municipality itself. The mode of detection predominated through referral 431 (83,8%), spontaneous demand 12 (2,3%) and highlighting nine (1,7%) cases detected through contact examinations, 55 (25%) notifications did not describe this information, and nine (4,1%) showed decertification in other ways.

In the univariate analysis model, the results show that men arrive at the service to be diagnosed with a greater number of injuries (p-value <0,05), with the clinical forms dimorphic and virchowian, that is MB (p-value <0,05) and with Disabilities Grade 1 and 2 denoting neural injury and/or physical disabilities already installed (p-value <0,05). The association between socio-demographic variables revealed that education, race and area of residence do not interfere with clinical variables such as: number of injuries and nerves affected, in the clinical form and operational classification, and in the degree of disability of WHO (value- p> 0,05). The age variable showed that the greater the age, the greater the number of lesions found in the diagnosis (p-value = 0,03), the greater the possibility of presenting the MB forms, that is, the dimorphic and virchowian clinical forms of the disease (p = 0,01) and have physical disabilities (p-value = 0,00).

In the final model of multivariate analysis performed by means of logistic regression, significance was found for the association between the presence of physical disabilities and being diagnosed in the clinical forms dimorphic and virchowian, being over 52 years old and more than 3 injuries at the time of diagnosis. Operational classification and gender do not influence the presence of physical disabilities.

Table 1. Association between clinical characteristics and average age of leprosy cases reported in São José do Rio Preto, SP, Brazil, from 2001 to 2016.

Variáveis	Média Idade	Desvio-Padrão	Valor-p
Classificação Operacional			
Paucibacilares (n=165)	46,26	16,97	0,0191
Multibacilares (n=349)	50,47	15,39	
Grau de incapacidades*			
Grau 0 (n=281)	45,90	16,33	
Grau 1 (n=157)	53,19	14,18	0,000
Grau 2 (n=49)	53,59	14,54	

* Missing data. Source: Notifiable Diseases Information System (SINAN)

Table 2. Variables independently associated with physical disabilities according to the WHO (Grades 1 and 2) of São José do Rio Preto, SP, Brazil from 2001 to 2016.

Variáveis	Odds Ratio Ajustado	IC 95%	P-Value
Classificação Operacional (multibacilar)	**1,00**	**0,43-2,30**	**0,9965**
Sexo (masculino)	1,11	0,73-1,68	0,6076
Forma Clínica (dimorfa e virchowiana)	1,66	1,10-2,51	0,0157
Idade (maior que 52 anos)	**1,03**	**1,01-1,04**	**0,0000**
Número de Lesões (mais que três)	1,04	1,01-1,07	0,0019

IC - Intervalo de confiança (Confidence interval) of 95%; * Multivariate analysis using unconditional logistic regression. Source: Notifiable Diseases Information System (SINAN).

DISCUSSION

A Brazilian study reports that the drop in the leprosy prevalence indicator in Brazil is related to differences in development and standard of living between regions, implying that early detection and reduction of disabilities are related to the efficiency of primary health care services. [18]

The association between socio-demographic variables revealed that education, race and area of residence do not interfere with clinical variables such as: number of injuries and affected nerves, in the clinical form and operational classification, and in the degree of disability of WHO. The age variable shows that the greater the age, the greater the number of lesions found in the diagnosis, the greater the possibility of presenting the MB forms and presenting physical disabilities. Contrary to the findings, research reports that the occurrence of the condition may be related to sociodemographic variables, as they live in clusters and share situations of poverty, with a high rate of transmission, since unfavorable socioeconomic conditions and poor housing conditions influence the risk to acquire the disease. [19-21]

In endemic regions, the age range

and living conditions were determining factors for the persistence of the disease and increased infectivity in a pediatric population. [19] In this investigation, the men arrived at the service to be diagnosed with a greater number of injuries, MB classification and with a degree of disability 1 and 2, showing neural injury and/or physical disabilities already installed. This finding was similar to multicentric research on risk factors for leprosy disability in India, also considered an endemic country, as well as the delay of the patient to the health services and the health professional in making the diagnosis. [22] Late diagnosis remains one of the challenges for controlling endemic diseases in underdeveloped countries.

In the multivariate analysis performed by means of logistic regression, statistical significance was found for the association between the presence of physical disabilities and being diagnosed in the clinical forms dimorphic and virchowian, being over 52 years old and more than 3 injuries at the time of diagnosis. Operational classification and gender do not influence the presence of physical disabilities.

Currently, it is observed that although there is a tendency to eliminate leprosy at the national level, regional disparities result in the maintenance of circulating disease. And this study is in line with the investigations, since in the endemic regions the risk factors are mostly referenced to social, economic and demographic conditions. [2,18,19,22,23]

In view of the risk factors, contact control becomes one of the strategic pillars for carrying out effective surveillance. and to train health professionals to improve health system records, in addition to optimizing information to analyze root causes and work with a focus on determinants. [24,25] In an attempt to achieve the WHO strategic plan [6], the municipality encourages the decentralization policy for primary care, the implementation of control actions through the Family Health Program (PSF), in addition to health education for professionals and the general population.

Over the past decade, research into the behavior of the disease and prevention and education actions in the municipality have been intensified in an attempt to improve the epidemiological profile, and have been carried out successfully by the teams, which shows a strong commitment by all professionals to the search for improvements in the clinical and epidemiological perspective of the patient and, therefore, the municipality.

CONCLUSION

In this study, it was found that sex (male) and age (older people) have a higher risk of leprosy infection. In the period and municipality studied, the predominance of male patients is observed, in the average age, with greater clinical and physical involvement. Sociodemographic risk factors did not show significance in clinical variables.

In order to reduce the risk of evident exposure, the municipality's program must emphasize the awareness of the male community, with a focus on key messages to attract the target audience, establish strategies for active search of cases and of communicators; as well as training, periodically, all health professionals for diagnosis and early treatment to break the chain of disease transmission, in addition to preventing physical disabilities (eyes, hands and feet), stigma, prejudice and discrimination. ■

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