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Original article

Health-related quality of life evaluated by Pediatric Quality of Life Inventory 4.0 in pediatric leprosy patients with musculoskeletal manifestations

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ABSTRACT

Objective: To evaluate the health-related quality of life (HRQL) in pediatric leprosy patients.
Methods: A cross-sectional study included 47 leprosy patients and 45 healthy subjects. The HRQL was measured by Pediatric Quality of Life Inventory 4.0 (PedsQL 4.0), and evaluated physical, emotional, social and school domains. The leprosy patients were classified by Ridley and Jopling classification criteria and assessed according to clinical musculoskeletal manifestations, laboratory and radiographic examinations.
Results: The median of current age was similar in leprosy patients and controls [12 (6–18) vs. 15 (5–18) years, $p = 0.384$], likewise the frequencies of female gender ($p = 0.835$) and middle/lower Brazilian socio-economic classes ($p = 1.0$). The domain school activities according the child-self report was significantly lower in leprosy patients compared to controls in the age group of 13–18 years [75 (45–100) vs. 90 (45–100), $p = 0.021$]. The other domains were alike in both groups ($p > 0.05$). At least one musculoskeletal manifestation (arthralgia, arthritis and/or myalgia) was observed in 15% of leprosy patients and none in controls ($p = 0.012$). Further comparison between all leprosy patients showed that the median of the physical capacity domain [81.25 (50–100) vs. 98.44 (50–100), $p = 0.036$] and school activities domain by child-self report [60 (50–85) vs. 80 (45–100), $p = 0.042$] were significantly lower in patients with musculoskeletal manifestations compared to patients without these manifestations. No differences were evidenced between the other HRQL parameters in both groups, reported by patients and parents ($p > 0.05$).
Conclusions: Reduced physical capacity and school activities domains were observed in pediatric leprosy patients with musculoskeletal manifestations.

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Qualidade de vida relacionada à saúde avaliada pelo Inventário Pediátrico de Qualidade de Vida 4.0 em pacientes pediátricos com hanseníase e manifestações musculoesqueléticas

Palavras-chave:
Lepra
Criança
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Artrite

RESUMO

Objetivo: Avaliar a qualidade de vida relacionada à saúde (QVRS) em pacientes pediátricos com hanseníase.
Métodos: Estudo transversal com 47 pacientes com hanseníase e 45 indivíduos saudáveis. A QVRS foi mensurada pelo Pediatric Quality of Life Inventory 4.0 (PedsQL 4.0) e os domínios físico, emocional, social e escolar foram avaliados. Os pacientes com hanseníase foram classificados pelos critérios de Ridley e Jopling e avaliados de acordo com manifestações clínicas musculoesqueléticas, laboratoriais e exames radiográficos.
Resultados: A média de idade atual foi similar em pacientes com hanseníase e controles [12(6-18) vs. 15(5-18) anos, p = 0,384], assim como frequências do sexo feminino (p = 0,835) e classes socioeconômicas brasileiras média/baixa (p = 1,0). De acordo com a auto-avaliação da criança relacionado com as atividades escolares, este domínio foi significativamente menor nos pacientes com hanseníase em relação aos controles de 13-18 anos [75(45-100) vs. 90(45-100), p = 0,021]. Os outros domínios foram semelhantes em ambos os grupos (p > 0,05). Pelo menos uma manifestação musculoesquelética (artralgia, artrite e/ou mialgia) foi observada em 15% dos pacientes com hanseníase e nenhuma nos controles (p = 0,012). Uma comparação mais detalhada entre pacientes com hanseníase mostrou que a mediana do domínio de capacidade física [81,25(50-100) vs. 98,44(50-100), p = 0,036] e de atividades escolares pela auto-avaliação da criança [60(50-85) vs. 80(45-100), p = 0,042] era significantemente menor nos pacientes com manifestações musculoesqueléticas em comparação com a dos pacientes sem essas manifestações. (1) Nenhuma diferença foi evidenciada entre os outros parâmetros de QVRS em ambos os grupos relatados pelos pacientes e pais (p > 0,05).
Conclusões: Diminuições dos domínios capacidade física e escolar foram observados em pacientes com hanseníase pediátrica e manifestações musculoesqueléticas.

Introduction

Leprosy, also known as Hansen's disease, is caused by the *Mycobacterium leprae*.[1] This is a relevant infectious disease in developing countries. Recently in Brazil, 6.7% of newly detected leprosy cases were diagnosed in children and adolescents.[2]

The clinical features of pediatric leprosy include several skin lesions, numbness of the skin, damage of peripheral nerves, arthralgia and arthritis.[3–11] In this regard, we recently detected that musculoskeletal manifestations were associated with severe leprosy in children and adolescents, especially in patients presenting nerve function impairment and neuropathy.[12]

Furthermore, adult leprosy patients could present reduced scores of health-related quality of life (HRQL), particularly in physical capacity and social participation domains.[13–17] To our knowledge, HRQL was rarely reported in pediatric leprosy,[17] and the impact of musculoskeletal manifestations on HRQL was not previous investigated.

Therefore, the objectives of our study were to assess HRQL in leprosy patients and healthy controls using a generic instrument for children/adolescents and theirs legal guardians, and to evaluate the possible influence of presence of musculoskeletal manifestations in decreasing HRQL.

Patients and methods

A cross-sectional study was performed with 56 leprosy patients, which were followed-up at the Dermatology Unit of a tertiary hospital in Brazil. Out of them, the HRQL of 47 leprosy patients was systematically evaluated. All patients fulfilled the leprosy diagnosis according to National Leprosy Program guidelines[4] and Ridley and Jopling classification criteria.[18] Control group included 45 healthy children and adolescents of local school in Brazil. This study was approved by the Local Ethical Committee. Patients and controls and their legal guardians signed the informed consent form.

Methods

Demographic data

Demographic data included current age and gender. Brazilian socio-economic classes were classified according to the Associação Brasileira dos Institutos de Pesquisa de Mercados.[19]

Clinical assessment of leprosy

Clinical assessment of Hansen's disease was performed according to National Leprosy Program guidelines.[4]

The leprosy patients were also classified by Ridley and Jopling classification criteria: borderline–borderline (BB), borderline–lepromatous (BL), lepromatous–lepromatous (LL), borderline–tuberculoid (BT), tuberculoid–tuberculoid (TT) or indeterminate leprosy (IL).[18]

Clinical musculoskeletal manifestations

Musculoskeletal manifestations were defined according to: arthralgia (diffuse joint pain or tenderness without evidence of inflammation), arthritis (swelling within a joint, or limitation in the range of joint movement with joint pain or tenderness) and myalgia (muscle pain or tenderness in one or more limbs without evidence of inflammation). Arthritis were classified according to the number of joints [oligoarticular (lower or equal to 4 arthritis) and polyarticular (greater or equal to 5 arthritis)] and duration [acute (less than 6 weeks) and chronic (over or equal to 6 weeks)], articular distribution [symmetric or asymmetric], pattern of joint involvement [addictive, migratory and intermittent] and type of joint involvement [peripheral (large or small joints) and axial].

HRQL assessment

The HRQL was determined by the generic instrument: Pediatric Quality of Life Inventory 4.0 (PedsQL 4.0) validated to Brazilian Portuguese language, using different versions for three age groups 5–7, 8–12 and 13–18 years.[20,21] Two instruments were used in the present study: PedsQL 4.0 child-self report and PedsQL 4.0 parents report. The PedsQL 4.0 questionnaire includes problems in four multidimensional domains presented in the previous month, such as physical capacity, emotional aspects, social aspects and school activities. The 23 items were scored using a five-point scale in the groups of 8–12 years, 13–18 years and parents (0 – never, 1 – almost never, 2 – sometimes, 3 – often and 4 – almost always) and for children at the age of 5–7 years with a three-point scale (0 – never, 2 – sometimes and 3 – often). The sum of the total score varied from 0 to 100. A higher score indicated a better HRQL.[20,21]

Laboratory and radiographic examinations

Blinded laboratory exams were performed for the clinical and HRQL assessments. Antinuclear antibodies (ANA) were measured at study entry by indirect immunofluorescence on human cell epithelioma (HEp-2) cells (GMK, USA) and staining reactivity at ≥1:80. Anticardiolipin (aCL) isotypes IgG and IgM by enzyme-linked immunosorbent assay (ELISA) (Phadia, Sweden), cut-off value of 20 GPL and/or MPL. HLA B27 and rheumatoid factor (RF) detections were carried out by in-house real-time polymerise chain reaction assay (Arup Laboratories, USA) and by immunoturbidimetric assays (Wiener, Argentina, cut-off <20 UI/ml) respectively in patients and controls with arthralgia and/or arthritis. Conventional joint radiographies were carried out in patients and controls with arthralgia and/or arthritis, and classified as: decreased joint space, erosions and ankylosis.

Statistical analysis

Statistical analyses were performed using the statistics program SPSS. The non-parametric Mann–Whitney test was used to compare the continuous variables and presented as median (range). Differences in frequencies were assessed by Fisher's exact test for categorical variables. Values of p were set at 5% ($p < 0.05$) in all statistical tests.

Results

The median of current age was similar in leprosy patients and healthy controls [12 (6–18) vs. 15 (5–18) years, $p = 0.384$], likewise the frequencies of female gender (47% vs. 51%, $p = 0.835$). No differences were evidenced in middle/lower Brazilian socio-economic classes in both groups (91% vs. 93%, $p = 1.0$).

Table 1 – Demographic data, classification criteria, clinical manifestations, laboratory, radiography and treatments in leprosy patients.

Variables	Leprosy patients ($n = 47$)
Demographic data	
Current age, years	12 (3–18)
Female gender	25/47 (53)
Brazilian socio economic classes	
Middle/lower middles class	46 (92)
Ridley and Jopling classification criteria	
Borderline–borderline	21 (45)
Indeterminate	0 (0)
Tuberculoid	26 (55)
Lepromatous	0 (0)
World Health Organization (WHO) classification	
Multibacillary	21 (45)
Paucibacillary	26 (55)
Clinical manifestation	
Hypopigmented or reddish skin lesions with loss of sensation	47 (100)
Erythema nodosum leprosum	0 (0)
Peripheral silent neuropathy	2 (4)
Arthralgia	1 (2)
Myalgia	3 (6)
Arthritis	5 (11)
Laboratory	
Autoantibodies	
Antinuclear antibodies (ANA)	1 (2)
Rheumatoid factor	2/5 (20)
IgM anticardiolipin (aCL)	7 (15)
IgG aCL	1 (2)
Radiography	
Joint radiographies abnormalities	0 (0)
Treatments	
Prednisone	8 (17)
Rifampicin, dapsone and clofazimin	21 (45)
Rifampicin and dapsone	26 (55)

Results are shown in media (range) and n (%).

Table 2 – Pediatric Quality of Life Inventory 4.0 (PedsQL 4.0) scores of three age groups according to reports of patients with leprosy and healthy controls and their parents.

Variables	Leprosy ($n=47$)	Controls ($n=45$)	p
5–7 years	($n=4$)	($n=6$)	
Physical (Patients)	100 (81–100)	98.44 (88–100)	0.719
(Parents)	98.44 (90.63–100)	98.44 (90.63–100)	1.0
Emotional (Patients)	65 (60–80)	75 (50–90)	0.515
(Parents)	65 (60–80)	72.50 (60–85)	0.504
Social (Patients)	85 (70–90)	82.50 (80–90)	0.909
(Parents)	95 (80–100)	90 (70–95)	0.321
School (Patients)	95 (80–100)	75 (50–100)	0.128
(Parents)	92.50 (75–95)	67.50 (45–95)	0.130
8–12 years	($n=20$)	($n=12$)	
Physical (Patients)	95.94 (63–100)	100 (88–100)	0.504
(Parents)	100 (68.75–100)	100 (90.63–100)	0.982
Emotional (Patients)	70 (55–100)	75 (45–100)	0.708
(Parents)	70 (55–100)	72.50 (65–95)	0.569
Social (Patients)	90 (75–100)	90 (45–100)	0.270
(Parents)	95 (35–100)	100 (45–100)	0.691
School (Patients)	80 (60–95)	85 (40–100)	0.346
(Parents)	80 (50–100)	87.50 (45–100)	0.281
13–18 years	($n=23$)	($n=27$)	
Physical (Patients)	93.75 (50–100)	93.75 (50–100)	0.597
(Parents)	100 (50–100)	93.75 (53.13–100)	0.179
Emotional (Patients)	70 (30–95)	75 (40–100)	0.358
(Parents)	75 (35–100)	80 (25–100)	0.769
Social (Patients)	90 (45–100)	95 (75–100)	0.506
(Parents)	100 (75–100)	100 (65–100)	0.631
School (Patients)	75 (45–100)	90 (45–100)	**0.021**
(Parents)	80 (35–95)	80 (35–100)	0.473

Results are presented in median (range) by Mann–Whitney test.

Table 3 – Pediatric Quality of Life Inventory 4.0 (PedsQL 4.0) scores of children and adolescents, and their parents according to the presence of musculoskeletal manifestations.

Variables	With musculoskeletal manifestations ($n=7$)	Without musculoskeletal manifestations ($n=40$)	p
Children			
Physical	81.25 (50–100)	98.44 (50–100)	**0.036**
Emotional	65.00 (30–80)	70 (45–100)	0.270
Social	90.00 (65–100)	90 (45–100)	0.336
School	60.00 (50–85)	80 (45–100)	**0.042**
Parents			
Physical	90.63 (50–100)	100 (68.75–100)	0.143
Emotional	65.00 (35–80)	72.50 (50–100)	0.107
Social	95.00 (80–100)	100 (35–100)	0.735
School	70 (50–95)	82.50 (35–100)	0.094

Results are presented in median (range) by Mann–Whitney test.

Demographic data, classification criteria, clinical manifestations, laboratory abnormalities, radiography and treatments in leprosy patients were described in Table 1.

Table 2 includes PedsQL 4.0 scores for three age groups of children and adolescents with leprosy and healthy controls and their parents. The domain school activities according the child-self report was significantly lower in leprosy patients compared to healthy controls in the age group of 13–18 years [75 (45–100) vs. 90 (45–100), $p=0.021$] (Table 2). The other domains were alike in both groups ($p>0.05$). All domains were also similar in the parent evaluations ($p>0.05$, Table 2).

At least one musculoskeletal manifestation (arthralgia, arthritis and/or myalgia) was observed in 15% of leprosy patients and none in healthy controls ($p=0.012$). Five leprosy patients had acute or chronic peripheral, asymmetric, migratory polyarthritis of small joints of the hands (metacarpophalangeal and proximal interphalangeal joints), with median duration of 12 months (ranged from 15 days to 36 months). Four of them had borderline–borderline leprosy form and had chronic polyarthritis with morning stiffness, mimicking juvenile idiopathic arthritis (JIA). ANA and HLA B27 test were negative in all patients with arthralgia and/or arthritis. RF was positive in 2 of 5 patients with arthralgia and/or arthritis. None of them had conventional joint radiographies abnormalities.

Further comparison between all leprosy patients showed that the median of the physical capacity domain [81.25 (50–100) vs. 98.44 (50–100), $p=0.036$] and school activities domain by child-self report [60 (50–85) vs. 80 (45–100), $p=0.042$] were significantly lower in patients with musculoskeletal manifestations compared without these manifestations. No differences were evidenced between the other HRQL parameters in both groups, reported by patients and parents ($p>0.05$, Table 3).

Discussion

To our knowledge this was the first report that studied HRQL in pediatric leprosy patients with musculoskeletal manifestations, and observed reduced scores in physical and school domains.

The major advantage of this study was the systematic assessment of the HRQL in children and adolescents with leprosy in a well-known endemic area of this infectious disease in Brazil. Moreover, a healthy control group with similar age, gender and socio-economic class was included in the present study. The importance of these similarities observed herein was also reported in several studies that found a relation between HRQL and low socio-economic class, gender and age.[22–24] The main limitations were the small number of leprosy patients evaluated herein and the use of only one HRQL generic instrument.

The global prevalence of leprosy is increasing around the world[2] and continues to be high endemic in a number of developing countries, including Brazil.[3] In 2012, the proportion of children and adolescents among newly detected cases in Brazil was 6.7%.[2] The main clinical involvements of leprosy are hypo pigmented or reddish localized skin lesions with loss of sensation and peripheral nerves involvements.[3] Musculoskeletal is the third most involved commonly organ/system in adult leprosy,[7] and arthritis was observed in up to 65%.[6,25,26] In pediatric leprosy population, we recently observed that musculoskeletal manifestation was associated with nerve dysfunction. Therefore, Hansen's disease should be included in the differential diagnosis of non-erosive asymmetric arthritis.[12]

Moreover, the scores of HRQL may be decreased in children and adolescents with chronic diseases comparing to healthy subjects,[27] as observed in our study. Interestingly, around 60% of the adult patients with leprosy experienced a limitation in the execution of daily activities and also 60% leprosy patients had problems in social participation.[16]

Furthermore, adult leprosy patients presented problems in mobility, interpersonal relationship, marriage, employment, leisure activities and social attendance.[13] In patients with 10–29 years, there was observed a lower HRQL scores comparing to healthy controls, in several categories, such as psychical, vitality, social functioning and emotional role.[17]

The present study investigated HRQL in three different groups of age of pediatric leprosy using PedsQL 4.0 score. In contrast with other questionnaires, such as SF-36 instrument, which assesses physical and mental components in adults, PedsQL 4.0 evaluates emotional domain and school activities, which are relevant to the pediatric population. A significant lower child-reported HRQL scores was observed in pediatric leprosy patients with musculoskeletal manifestations in comparison with patients without these manifestations in the domains physical capacity and school activities. These findings could be related to neuropathy and/or articular chronic pain with writing difficulties, which induces chronic health problems and poor school performance.[28] On the other hand, no differences were evidenced in the emotional and social domains, probably due to the predominance of skin localized manifestations in our population, without findings of stigmatized disease. Indeed, none of our patient had a severe lepromatous subtype, which is characterized by nodules (lepromas) and a peculiar facies with diffuse infiltration and eyelash loss, named leonine facies.[3,4]

Therefore, a detailed investigation of all leprosy patients with musculoskeletal manifestations is required. The need to establish preventive programs, including a multiprofessional and a multidisciplinary team, is of the utmost importance for this population.

In conclusion, this was the first study to identify reduced physical capacity and school activities domains in pediatric leprosy patients with musculoskeletal manifestations.

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Conflicts of interest

The authors declare no conflicts of interest.

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