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ORIGINAL PAPER

Pediatric rheumatology interconsultation: sample from a tertiary hospital in southern Brazil

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Abstract

Objective: To describe the clinical-epidemiological profile of pediatric patients seen via inter-consultation in a pediatric rheumatology (PR) outpatient clinic. **Methods:** Cross-sectional and observational study that analyzed the medical records of patients seen in the form of inter-consultations in a PR outpatient clinic of a tertiary hospital for 14 months. Epidemiological, clinical history and laboratory tests data were collected and descriptive statistics were performed. **Results:** we included 37 patients, 27 (73%) females and 10 (27%) males, with a median age of 12.4 years (min: 1.3 max: 15.9). After several complementary exams, the patients were referred by 13 different specialties, with a predominance of pediatric dermatology. In the first consultation with a pediatric rheumatologist, the main complaints were arthralgia (51.3%), skin blemishes (32.4%) and skin rash (29.7%). The period between symptoms onset and the consultation ranged between 16 and 4,554 days, with a median of 730 days. Twenty (54.1%) patients had the exclusion of a rheumatological disease, three (8.1%) lost follow-up and 14 (37.8%) were diagnosed with rheumatological diseases, the most common being linear scleroderma (28, 6%), juvenile systemic lupus erythematosus (28.6%), juvenile idiopathic arthritis (14.3%) and juvenile dermatomyositis (14.3%). **Conclusions:** The main complaints of patients referred to PR were arthralgia and skin lesions, with a long period of symptom evolution, in addition to a wide age range and the predominant role of female patients. In addition, prior to the pediatric rheumatologist evaluation, the patients consulted several specialties and were exposed to several complementary exams.

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INTRODUCTION

Pediatric rheumatology (PR) is the medical specialty that deals with a wide and heterogeneous set of autoimmune and auto-inflammatory diseases in children and adolescents. In addition to being painful and limiting, these can cause permanent physical restrictions, reduced quality of life, reduced participation in social activities and less participation in the job market, in addition to high costs to healthcare systems and even death[1,2].

However, PR has only 171 certified professionals with a field of expertise in pediatric rheumatology according to the Brazilian Society of Pediatrics, consecrated as one of the smallest and most recent pediatric subspecialties, being unknown by doctors and society[3,4]. In this context, epidemiological studies on rheumatological diseases in childhood and adolescence are scarce, including few patients and had low external validity. This characterizes a problem, since these studies are fundamental to alert healthcare professionals to early diagnoses, provide a substrate for the study of racial, genetic and demographic factors associated, reveal targets for treatments and the natural course of diseases, as well as point out needs of healthcare managers[5].

Accordingly, the objective of this study, carried out through the analysis of medical records, is to describe the clinical-epidemiological profile of patients treated for 14 months, in the form of interconsultations, in a pediatric rheumatology outpatient clinic of a tertiary hospital in southern Brazil.

METHODS

The study was carried out in a tertiary university hospital, located in southern Brazil, which acts as a regional reference for several specialties. In May 2018, a pediatric rheumatology outpatient clinic was opened in this hospital with the aim of serving children and adolescents with demands in this field through consultations with other pediatric specialties of the institution. The service is carried out exclusively via consultations in this outpatient clinic due to the characteristics of the contract between the hospital and its contractors.

With a cross-sectional, observational and individualized design, the study was carried out through a retrospective analysis of the medical records of patients seen at this outpatient clinic between May 2018 and June 2019. Information was collected by a single researcher between April and August 2019 and aggregated into Microsoft Excel spreadsheets.

The medical records were accessed at the hospital's medical file service and identification data, clinical history and complementary exams were collected. The data obtained fell within the period of time between the patient's entry into the healthcare service and the establishment of a defined outcome in the PR outpatient clinic. An outcome was defined as the evolution in the patient's medical record of a diagnosis of rheumatologic disease or outpatient discharge.

Clinical conditions that are usually managed by a pediatric rheumatologist were considered rheumatologic diseases, with patients classified according to the international diagnostic criteria of the main rheumatologic diseases in childhood and adolescence. For laboratory tests, erythrocyte sedimentation rate and C-reactive protein tests were considered as evidence of inflammatory activity, as an examination of the immune system, serum complement and serum immunoglobulin levels, and as autoantibodies, antinuclear factor, anti-neutrophil cytoplasm, antiphospholipid antibodies, anti-aminoacyl-tRNA synthetase antibodies, anti-centromere antibody and anti--Scl-70 antibody. For skin lesions, we used the concept of stain for changes in skin color, without associated changes in relief. On the other hand, skin rash was considered as a skin lesion composed of erythema, associated with papules or pustules.

Descriptive statistics were performed using the statistical software R (R Core Team, 2019) version 3.6.1, so that the results of quantitative variables were described by means, standard deviations, medians, minimum and maximum values. For categorical variables, frequencies and percentages were presented. The study was approved by the institution's human research ethics committee.

RESULTS

WE studied the medical records of 37 patients, 27 (73%) were females and 10 (27%) were males, with a median age at admission to the PR clinic of 12.4 years (min: 1.3 max: 15.9). Of the total, 15 patients (40.5%) were from the state capital, 10 (27.1%) from the metropolitan region and 12 (32.4%) from cities in the interior.

Several specialties were responsible for requests for consultations for pediatric rheumatology, with pediatric dermatology being predominant, accounting for 35.1% of the cases. Table 1 shows the percentage of each specialty among the PCs received by the pediatric rheumatology outpatient clinic in the studied period. The period between the onset of symptoms and consultation with the specialist ranged from 16 to 4554 days, with a median time of 730 days.

Table 1 - Frequency of referrals by specialty in the pr outlet.

Specialty	Absolute frequency	Relative frequency (%)
Pediatric dermatology	13	35.1
Pediatric oncology	5	13.5
Pediatric allergology	4	10.8
Pediatric nephrology	3	8.1
Pediatric Infectology	3	8.1
General pediatrics	2	5.4
Emergency department	2	5.4
Intensive care unit	1	2.7
Rheumatology	1	2.7
Pediatric pneumology	1	2.7
Pediatric neurology	1	2.7
Pediatric endocrinology	1	2.7

Most patients had complementary exams prior to the rheumatological evaluation: 31 (83.8%) had undergone a blood count, 30 (81.1%) had inflammatory activity tests, 20 (54%) had undergone an immune system test and 13 (35, 1%) dosage of autoantibodies. In addition, 15 (40.5%) of them had undergone an ultrasound, 12 (32.43%) had an X-ray, nine (24.3%) had a CT scan and five (13.5%) had an MRI.

Several clinical complaints were reported during consultation with a pediatric rheumatologist. The most common were arthralgia and skin lesions, with the main symptoms reported in Table 2.

Table 2 - Patients' complaints at the entry of the pr center.

Complaint	Absolute frequency	Relative frequency (%)
Arthralgia	19	51.3
Skin spot	12	32.4
Skin rash	11	29.7
Musculo-skeletal pain	10	27
Fever	8	21.6
Mouth ulcers	6	16.2
Alopecia	5	13.5
Abdominal pain	3	8.1
Eye issues	2	5.4
Headache	2	5.4
Weight loss	1	2.7

Among the 19 patients with arthralgia, the lower limbs were responsible for most cases, with 12 (63.1%) patients reporting knee pain and seven (36.8%) ankle pain. In addition, the upper limbs were also affected, with six (31.6%) patients with pain in the hands and three (15.8%) in the elbow.

After clinical evaluation, laboratory investigation at the PR outpatient clinic was performed with blood count in 20 (54%) patients, tests of inflammatory activity in 31 (83.8%), autoantibody measurement in 27 (73%) and immune examination in 19 (51.3%). The anti-nuclear factor (ANA) was requested for 22 (59.4%) patients and proved to be reactive in 10 (45.4%), with titers varying between 1/80 and 1/640. Among the imaging tests, two (5.4%) patients underwent magnetic resonance imaging, two (5.4%) underwent ultrasound and one (2.7%) underwent radiography.

After the first consultation, three patients lost outpatient follow-up, so that only 34 had a defined outcome. Of these, 14 (41.2%) were diagnosed with rheumatologic diseases and 20 (58.8%) had a non-rheumatologic condition as an outpatient outcome. Among the latter, 15 (75%) had the exclusion of a rheumatologic patient as an outcome. Table 3 illustrates patient outcomes at the outpatient clinic.

Table 3 - Outcomes in the pr ambulatory.

Outcome	Absolute frequency	Relative frequency (%)
RHEUMATOLOGICAL CONDITIONS		
Linear scleroderma	4	28.6
Juvenile systemic lupus erythematosus	4	28.6
Juvenile idiopathic arthritis	2	14.3
Juvenile dermatomyositis	2	14.3
Juvenile fibromyalgia	1	7.1
Reactive arthritis	1	7.1
NON RHEUMATOLOGICAL CONDITIONS		
Rheumatological disease ruled out	15	75
Mechanical alteration	3	15
Unspecific limb pain	2	10

SOURCE: The author (2019)

With the definition of the outcome in the PR outpatient clinic, several approaches were adopted. Among the 34 patients who maintained outpatient follow-up, 20 (58.8%) were prescribed a pharmacological treatment. Of these, disease-modifying antirheumatic drugs (DMARDs), indicated for seven (35%) patients, were the most used. The DMARDs used were Methotrexate and Hydroxychloroquine. In addition, non-steroidal anti-inflammatory drugs were prescribed for four (20%) patients, immunosuppressive drugs for three (15%), tricyclic antidepressants for one (5%) and antiplatelet drugs for one (5%). In addition, four (20%) patients were prescribed vitamin D supplementation. The immunosuppressive drugs used were Mycophenolate mofetil, Tacrolimus and Cyclophosphamide.

DISCUSSION

In a national scenario of scarce epidemiological studies in pediatric rheumatology, this study demonstrates the clinical and epidemiological characteristics of patients treated as interconsultations in a tertiary hospital in southern Brazil, contributing to the elucidation of the main characteristics of patients treated by the specialty in our country.

In our study, the vast majority of patients were females, accounting for 73% of consultations. This result can be partially explained by the fact that the conditions most diagnosed in the outpatient clinic are more prevalent in females[6,7]. In the literature, data on gender predominance are variable, with case series demonstrating a predominance of females, males, and equality between males and females, with the preponderance mainly determined by the prevalence of different diseases in the regions[8,9].

In childhood-onset autoimmune diseases, sexual bias is generally less evident than in adults, probably due to different hormone levels, with estrogens being strongly involved in the development of autoimmunity[10]. Even so, some rheumatic conditions, such as idiopathic arthritis (JIA), show a strong predilection for girls, and differences may exist between men and women in the outcome of the disease.

For example, JIA-associated chronic anterior uveitis most commonly affects girls, but boys tend to have a more severe course[11].

As rheumatologic diseases in childhood and adolescence constitute a heterogeneous group of more than 150 clinical conditions, patients of different ages are seen by a pediatric rheumatologist. The range from 1.3 to 15.9 years found in our study, with a median of 12.4 years, is consistent with what has been demonstrated in the African, Asian, European and North American continents[9,12–14].

Likewise, in the literature, the time elapsed between the onset of symptoms and consultation with a pediatric rheumatologist is variable. North American data show an average interval of 12.6 ± 20.3 months, in line with that shown in Nigeria, with an average interval of 18.4 ± 9 months[13,15]. In Yemen, the median time recorded was 12 months (min: 0.13 max: 98.4), while in our study this time was 24.3 months (min: 0.5 max: 151.8)[16].

One of the possible explanations for this finding is the impossibility of referring patients to the PR that existed before the opening of the outpatient clinic studied, causing them, even with symptoms suggestive of rheumatologic diseases, to remain trapped in the specialty of origin. In addition, in the aforementioned studies, patients were referred directly from primary care to the RP reference center, a dynamic different from what occurred in our hospital, in which consultations took place in the form of interconsultations in a tertiary hospital. This dynamic meant that the pediatric rheumatologist was, at least, the third physician to assess the patient, and this may be another factor that contributed to a longer interval between the onset of symptoms and consultation with the specialist.

In our study, in line with what has been demonstrated in the literature, 13 different specialties were responsible for referrals. In addition, pediatric dermatology was the specialty that authored most referrals.

This finding may be a reflection of the strong interrelationship between rheumatology and dermatology, which share the management of several diseases[17]. Accordingly, the literature discusses the creation of shared clinics between specialties, aiming to reduce the number of medical consultations, which patients are submitted and standardize the prescription of treatments[18,19]. In view of our results, studies that assess the effectiveness of these shared clinics in our environment may be useful, since most patients in our series traveled great distances to the medical center.

The multisystemic character of rheumatologic diseases can also be observed by analyzing the main complaints of patients at the entrance to the outpatient PR clinic. In our study, the main diagnoses were juvenile systemic lupus erythematosus (JSLE) and linear scleroderma, the main symptoms reported by patients were arthralgia and skin lesions. In the study conducted by Karadag et al. in Turkey, whose main diagnosis was human auto--inflammatory syndromes, the main symptoms described were arthralgia and recurrent fever associated with abdominal pain[20]. Similarly, in a study carried out in Yemen by Haifa Dahman, the main symptoms reported were arthralgia, joint edema and fever, in a scenario where the most common diseases were JIA and JSLE[16]. These data suggest that the symptoms most reported by patients in pediatric rheumatology services are related to the diseases more incidental in the region, but that arthralgia always plays an important role in the series.

As rheumatologic diseases in childhood and adolescence are rare conditions, but which make a differential diagnosis with common clinical conditions, the establishment of criteria for referral to a pediatric rheumatologist is a complex task. This may partially explain the high rates reported in the literature of non-rheumatological conditions referenced to the specialty. In our study, only 41.2% of referrals had a rheumatologic condition as an outcome, a figure comparable to the 40.5% reported in the USA, 31.6% in Canada, 40% in Nigeria, 52.3% in Turkey and 51, 2% in Israel[15,20]. Another factor that may contribute to these data is the low knowledge of physicians regarding the assessment of the musculoskeletal system, causing benign and self-limiting conditions, which should be managed in a first clinical care, to be referred for evaluation by the specialist[21].

The Brazilian Society of Pediatrics (SBP), through an adaptation of criteria developed by the American College of Rheumatology in 1997, suggests that a patient be referred to pediatric rheumatology when he/she has a prolonged fever of undetermined origin, loss of function in the osteoarticular system, joint pain or swelling with no apparent cause, abnormal rheumatologic laboratory tests and suspected autoimmune disease, in addition to diagnostic evaluation and long-term follow-up of children and adolescents with suspected or definitive diagnoses of rheumatologic diseases[22].

All patients evaluated in our study met the criteria suggested by the SBP. However, 32.4% of the patients reported skin spots at the first consultation and 29.7% a skin rash. These manifestations, despite being common and with great evidence in the literature, are not in the referral criteria postulated by the SBP[23]. Thus, there is a need for national epidemiological studies to strengthen the findings of the present study, providing substrate for possible updates of the referral criteria, making them more suitable for our environment.

It is known that rheumatologic diseases have a varied incidence in different parts of the globe, with the interference of several factors, such as economic, demographic and ethnic ones[24]. In the only Brazilian study with the incidence of these conditions in pediatrics, Maria Terreri et al. JIA, Henoch-Schönlein purpura and JSLE were, in this order, the diseases with the highest incidence in the state of São Paulo in 2010, in line with what has been reported in the world literature[25,26]. In our study, the low number of patients with rheumatologic diseases limits the comparability of findings. However, there is an important role of linear scleroderma, which is reported with low frequency in the world series. This condition is reported in 8.1% of patients in Yemen, 6.5% in Singapore, 1.7% in India and 0.9% in Thailand[8,9,16,27].

One of the hypotheses to explain the incidence of 28.6% in our study is due to the high number of patients who were referred by pediatric dermatology, since skin manifestations are predominant in this disease[28].

In addition, no patient was diagnosed with Henoch-Schönlein purpura, which was the most frequent rheumatologic disease in the study held by Tan et al in Singapore, and which plays an important role in pediatric rheumatology referral centers worldwide[23,27]. A probable reason for this is the self-limiting nature of the main manifestations of this vasculitis, which tend to disappear in a few weeks[29]. As most patients presented a time between the onset of symptoms and consultation with a pediatric rheumatologist of tens of months, even though the initial diagnosis was Henoch-Schönlein purpura, signs and symptoms of this condition would have disappeared at the time of admission to the clinic.

In conclusion, the demographic characteristics of the patients seen at the outpatient clinic studied were similar to those from other series worldwide. However, the incidence of reported diseases differed from that shown in the literature, as well as the time elapsed between the onset of symptoms and consultation with a pediatric rheumatologist. These data are possibly related to the consultation dynamics in which the patients in our study were seen.

One of the limitations of this study work is the retrospective data collection from medical charts, limiting the evaluation of the case to the evolution of the medical chart by the assistant physician, which may omit important characteristics. Another limitation is the dynamics of patient care in the form of consultations since this makes the analysis dependent on the characteristics of other hospital specialties.

In this sense, national epidemiological studies that assess patients referred directly from the health care network to the pediatric rheumatologist are useful in contributing to the understanding of epidemiology of rheumatologic diseases in childhood and adolescence. As the diseases in question are rare, national multicenter studies are suggested to increase the external validity of our findings.

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