Title:

Disease course and adult outcomes of childhood-onset rheumatic diseases

Introduction:

The burden of childhood-onset rheumatic diseases is difficult to be accurately established. Inconsistencies of definition and classification, the rarity of occurrence for many of these disorders and in many cases loss to follow-up of these patients, frequently due to change of medical care from pediatric into adult rheumatology, have prevented accumulation of substantial data concerning the outcome of these conditions. As increasing numbers of patients with these conditions survive and are followed into adulthood, understanding the clinical course of childhood rheumatic diseases and their effect on functional status, quality of life, education and professional activity, comorbidity (with a particular focus on cardiovascular health, bone health and fertility) and life expectancy are very relevant outcome parameters for which little information exists.

Over the past years a few studies have examined the outcomes of adults with childhood-onset rheumatic diseases and the impact of these conditions on long-term global health status, functional aspects and quality of life. As these studies have been focused primarily on limited data sets focused on Juvenile Idiopathic arthritis (JIA) and Systemic Lupus Erythematosus (SLE), with no in depth analysis of other conditions and long-term risks associated with treatment, this field continues to be poorly explored.

Our aim is to address adult outcomes of patients with childhood-onset rheumatic diseases registered on Reuma.pt, regarding disease course, functional impact, social impact, treatment adverse effects, comorbidities and mortality.

Objectives:

To evaluate the outcomes of patients with childhood-onset rheumatic diseases registered on Reuma.pt, as follows:

1) Disease course will be analyzed according to diagnosis and current disease status assessed through disease specific activity indexes; using both childhood and adult disease classifications, whenever applicable.
2) Functional impact will be evaluated through health assessment questionnaires.

3) Social outcomes will be assessed through marital status, education level and current employment status.
4) Adverse effects of therapy will be assessed and described.
5) Comorbidities and mortality will be analyzed through data registered in Reuma.pt.

Methods:

This will be a cross-sectional study with the following inclusion criteria: patients with childhood-onset rheumatic diseases registered in Rheumatic Diseases Portuguese Registry (Reuma.pt) that at the time of data analysis are more than 18 years old.

Data will be collected from Reuma.pt and will include patient demographics (age, gender and race), education level (years), employment status, marital status, diagnosis, pattern of disease onset, disease duration (years), comorbidities, current and previous therapy, with special emphasis on steroids, DMARDs and biological therapy.

Current disease status will be assessed through disease specific activity indexes evaluated at disease onset and at the last evaluation (joint counts and JADAS for first evaluation, joint counts and DAS 28 for patients latter on classified as rheumatoid arthritis, DAS 44 for psoriatic arthritis and peripheral spondyloarthritis patients, BASDAI and ASDAS for ankylosing spondylitis, SLEDAI for SLE). Serologic aspects (rheumatoid factor, ACPA antibodies, ANA) will be analyzed. For other rheumatic diseases, like scleroderma or dermatomyositis/polimyositis, current disease status (remission or still active disease) will be assessed through the information written in notes concerning disease activity. Participating centers will be asked to include in Reuma.pt cases of other connective tissue diseases that might be missing in the register. Functional and damage evaluation will be assessed by HAQ score or BASFI or SLICC, as appropriated. Treatment safety will be evaluated through side effects registry and reasons for discontinuation.

Associations will be made between possible predictive factors of adult outcome, such as age and pattern of disease onset, disease duration, duration of exposure to immunosuppressive treatments, with outcomes such as function and comorbidities.

Participating centers will be asked to identify pediatric cases lost for follow up in the last 10 years. If these cases were not registered in Reuma.pt this information will be added to the register. These cases will be crosschecked in order to verify if they were not later introduced in Reuma.pt by another center. After that centers will be asked to

contact the patient in order to invite him/her for a clinical interview (including disease activity, HAQ questionnaire and a comorbidities questionnaire) or at least to respond by phone to a HAQ questionnaire and a comorbidities questionnaire.

Expected size of the sample, based on a preliminary screen of Reuma.pt – 400 patients

Statistical analyses

Continuous covariates will be expressed in terms of their mean and standard deviation or median and interquartile range, as appropriate. Categorical covariates will be described by frequency distribution. Comparisons between groups of the covariates and the outcomes are going to be evaluated using chi2 tests for categorical data, while for continuous data, we will use the student's t-test or Mann-Whitney test as appropriate. The associations between continuous variables will be expressed as Spearman correlation coefficients to the non-normal distribution or as Pearson correlation coefficients for normal distribution. In all analyses $p< 0.05$ will be considered to be statistically significant. All calculations will be performed using the statistics program SPSS.

Expected results and possible limitations:

We expect to identify factors, like age and pattern of disease onset, disease duration, duration of exposure to immunosuppressive treatments, that may be related to poor function, more disability and more comorbidities.

Possible limitations of this study are the cross-sectional design, a potential selection bias in the inclusion of the patients by missing data in the registry and the analysis that may not be entirely representative of the whole population. In fact, patients with a better prognosis might be lost for follow up and patients with worse outcome will tend to seek continued medical care. To minimize this problem lost for follow up patients will be asked to be retrieved by centers.

Timeline for the project:

The project will start as soon as the dataset can be obtained. We expect to analyze the data until the end of 2014 and publication planned for 2015.

Research team:

Proponent: Filipa Oliveira Ramos

Supervisors: José António Melo Gomes e João Eurico Fonseca

Institutions involved: participation is open to all Portuguese centers interested in collaborating in this project. Co-authorship will be granted to a maximum of 2 co-authors per center, actively collaborating in the project. Co-authorship will be dependent on the number of patients enrolled (a minimum of 10 patients per participating center is required for 1 participating author and ≥20 patients for 2 authors) and on the involvement of the authors in the work to collect data and write the manuscripts.

Funding and conflicts of interest

No conflicts of interest and no external funding to declare.