

THE ISRAELI INTERNET-BASED REGISTRY: NOVEL CONCEPT OF MULTICENTER DATA COLLECTION IN PEDIATRIC RHEUMATOLOGY

Philip J Hashkes, MD, MSc, Yosef Uziel, MD, MSc, Moshe Rubenstein, BEd, Pnina Navon, MD, Shai Padeh, MD, Masza Mukamel, MD, Riva Brik, MD, Joseph Press, MD, Tsivia Tauber, MD, Liora Harel, MD, Yaacov Berkun, Judith Barash, MD

Philip J. Hashkes, MD, MSc, Cleveland Clinic Foundation, Cleveland, OH, USA
Yosef Uziel, MD, MSc, Sapir Medical Center, Kfar-Saba, Israel
Moshe Rubenstein, BEd, Safed, Israel
Pnina Navon, MD, Shaarei-Tzedek Medical Center, Jerusalem, Israel
Shai Padeh, MD, Shiba Medical Center, Tel-Hashomer, Israel
Masza Mukamel, MD, Schneider Children's Hospital, Petah-Tikva, Israel
Riva Brik, MD, Rambam Medical Center, Haifa, Israel
Joseph Press, MD, Soroka Medical Center, Beer-Sheba, Israel
Tsivia Tauber, MD, Assaf Harofeh Hospital, Zerifin, Israel
Liora Harel, MD, Schneider Children's Hospital, Petah-Tikva, Israel
Yaacov Berkun, MD, Bikur Holim Hospital, Jerusalem, Israel
Judith Barash, MD, Kaplan Medical Center, Rehovot, Israel
For the Pediatric Rheumatology Study Group of Israel

Source of Funding: This study was supported in part by a grant from the Technion, Israel Institute of Technology.

Key words: Pediatric rheumatology, epidemiology, registry, database

Corresponding author:

Philip Hashkes, MD
Dept. of Rheumatic Diseases A50
Cleveland Clinic Foundation
9500 Euclid Ave.
Cleveland OH 44195
Tel: 216-445-8525
Fax: 216-445-7569
Email: hashkep@ccf.org

ABSTRACT

Background: Pediatric rheumatology registries exist in several countries. The data collection process for most registries is cumbersome. It is usually paper-based, dependent on mail transmission, and needing additional personnel to enter the data into a computer. Results are not readily available to researchers. To make this process more efficient and to develop a national system we established an internet-based pediatric rheumatology registry.

Objective: To demonstrate the methodology of the Israeli internet-based pediatric rheumatology registry.

Methods and Results: In March 2001, we established an internet-based registry with the participation of all pediatric rheumatologists throughout Israel. Data are entered on new patients with a rheumatic condition. The data are entered on each physician's personal computer and include demographic data, referral source, rheumatologic diagnoses, drug, and disease progress data. Most data are entered by opening windows with the mouse, thus data entry is easy and quick.

Mechanisms exist to detect double entries and patients seen by other pediatric rheumatologists. Privacy is ensured by password entry, firewalls and lack of identifying features other than initials and date of birth. The data are automatically analyzed and updated for each physician's practice and for national statistics.

Results: Since the registry's establishment, data on nearly 3000 patients has entered, including >600 with various types of chronic arthritis, ~100 with systemic lupus erythematosus and ~100 with other connective tissue diseases. Several research projects are underway utilizing the database. All physicians note the ease of operation and the useful data generated for their practice.

Conclusion: We have demonstrated the feasibility of using the web for establishing a national registry. This model can be used as a template for other registries that may serve research purposes.

INTRODUCTION

Medical registries have several purposes. They assist to calculate the incidence and prevalence rates of important diseases. Descriptive and epidemiologic data can help formulate etiologic or pathogenic hypothesis. Registries can facilitate research projects, specifically multicenter clinical trials and disease outcome studies. Central registries enable rapid access to all patients with a specific diagnosis. Registries can assist public health authorities in the planning of health resources needed for a specific disease. Registries are especially important in a field such as pediatric rheumatology in which most diseases are relatively uncommon.

In several Western countries (United States, Canada, United Kingdom, Finland) multicenter pediatric rheumatology registries have been established [1-5]. In some of the less populated countries, with few centers of pediatric rheumatology, cooperation between all pediatric rheumatologists enabled the determination of incidence and prevalence rates of many common pediatric rheumatic diseases (Canada, Finland) [2,4,5]. In larger countries, complete cooperation was impossible. Regional registries, however, enabled local determination of disease frequencies (parts of United Kingdom, Sweden, Massachusetts, Minnesota [Mayo Clinic]) [3,6-10].

Registries have been established by 2 clinical trial organizations in pediatric rheumatology: the Pediatric Rheumatology Collaborative Study Group (PRCSG) in North America and the Pediatric Rheumatology International Trials Organization (PRINTO) based in Europe (Italy), which include centers from South America, Middle East, Asia, and Oceania. Several pediatric rheumatology disease-specific or drug-related registries have been established. These include registries for scleroderma (Italy), dermatomyositis (United States -US), outcomes of juvenile rheumatoid arthritis (US), vasculitis (Turkey), chronic infantile neurological, cutaneous and articular syndrome (CINCA, France) and patients treated with etanercept (Germany).

The data collection process for most registries is cumbersome. It is often paper based, dependent on mail/fax transmission, and needing additional personnel to enter the data into a computer. Results are not readily available to researchers. To make this process more efficient and to encourage increased physician participation we developed in Israel an internet-based national Pediatric Rheumatology Online Journal Vol. 2, No. 1 2004

pediatric rheumatology registry. Potential advantages of an internet-based registry include the ease of entering data at flexible times and locations, the ease of adapting data entry forms to changes (and correcting mistakes), assurance of better quality control, and the facilitation of communication with collaborators. This enables the database to be used nationally or internationally, with readily available and automatically updated results. One potential disadvantage is keeping patient data and identity private, an acute issue in countries, such as the US, that have recently passed patient privacy laws (SEE LINK www.hhs.gov/ocr/hipaa/).

In this paper we describe the development and workings of the Israeli Pediatric Rheumatology Registry.

METHODS

Eleven pediatric rheumatologists, representing almost all Israeli pediatric rheumatology clinics from Safed in Northern Israel to Beer-Sheba in the Negev participated in the registry. Data are entered on all new patients ≤ 18 years old with a pediatric rheumatology condition seen in outpatient clinics or inpatient consultation since March 1, 2001. Data were also entered on existing patients with significant chronic pediatric rheumatologic diseases. Data items collected are detailed in Table 1. (Also, view and practice using, data entry screen at www.moshe-r.net/pedrheumdemo. In order to maintain confidentiality, the name of the physician on this linked demonstration was changed, as well as the patients' date of birth (within 30 days) and initials. However, the results presented in the demonstration are based on actual registry data.

Data entry time is short and improves with practice after entering data on several patients. Most data are entered by opening windows of prepared lists. Open comments can be added at each physician's discretion. Diagnoses are based on accepted diagnostic and classification criteria when available, or on clinical judgment when diagnostic criteria are not available [11,12]. The initial diagnosis list was based on the US registry [1]. The master list of diagnoses can be changed and diagnoses added by agreement of the participating physicians. The system can accommodate changes to classification of diseases.

Physicians can change/cancel diagnoses or later add diagnoses. The previous diagnosis (if changed) will still show on the screen (in red) but will not be counted in the summary. In order to prevent double entries, the system recognizes patients with similar initials/birthday and will query the physician as to whether the patient is new or was previously entered. Also, there is a check-off box to indicate whether a patient was seen by other pediatric rheumatologists. The list can be obtained by the registry administrator (MR) and the physician responsible for the registry (JB, formally PJH).

The system also has safeguards for mistaken data entry. The system will recognize incorrect date entry, such as the date of clinic visit coming before the date of birth. Most mistakes are avoided by having queries answered by choosing from prepared lists.

There are several safeguards to ensure the privacy of patient data and to prevent patient identification. Entry to the system is limited by password. Firewalls exist to prevent outside invasion. Patients are identified only by initials and by date of birth. Each physician has devised a numerical code to enable later identification of the patients that he/she has entered. The Helsinki committee approved the registry and a waiver of individual informed consent was obtained. However, a separate Helsinki committee approval is necessary for any additional research project utilizing the registry.

The data are analyzed automatically and updated after each entry. Physicians can see summary data for their practice as well as national summary data. The summary includes demographic and disease-related data for each diagnosis and summary data for all patients. Also available are lists of patients sorted by date of entry, date of birth, date of clinic visit, initials and by diagnosis.

RESULTS

As of March 2003, data on 2984 patients with 3341 rheumatologic diagnoses were entered to the registry. Summary data for all patients is in Table 2. A partial list with the major diagnoses seen in our clinics is in Table 3. The full breakdown by diagnosis can be seen in the LINK TO

www.moshe-r.net/pedrheumdemo (select activity function: national demography report and national Pediatric Rheumatology Online Journal Vol. 2, No. 1 2004

summary data). In these functions the number of patients with each diagnosis can be seen as well as demographic data and disease related data. The breakdown of the practice of an individual physician can be accessed in several ways. There are list of patients by date of birth, initials and date of clinic visit (select activity: view patient table). The data on individual patients can be accessed by clicking on the initials. Also each physician can access a summary of his/her practice (select activity: my demography and my diagnosis reports). A breakdown of patients by diagnosis can be seen (select activity: patient list by diagnosis) as well as diagnoses that were later changed or cancelled (select activity: my cancelled diagnosis report).

Since the major purpose of this registry was epidemiologic, no automatic tabulation of drug use or progress data was done. For the same reason and also due to limited funds we did not collect more sophisticated drug and outcome data (such as quality of life measures).

Several research projects utilizing the registry have been started.

1. Calculation of the prevalence of common chronic pediatric rheumatic diseases in Israel.
2. Comparison of the clinical features of systemic lupus erythematosus (SLE) in children and adults, in collaboration with the Israeli adult SLE registry.
3. Description of the clinical, laboratory and outcomes of children with antiphospholipid antibody syndrome.
4. Description of the outcome and etiology of patients with recurrent transient hip synovitis.

The registry was utilized to establish a list of patients with SLE, antiphospholipid antibody syndrome and transient hip synovitis and their physicians. Patients were then fully identified by contacting their physicians. Confirmation of the diagnosis and further data collection were done by chart review.

Due to the nascent stage and novelty of this project we encountered several problems, mainly related to technical issues, the type of data to be entered and physician collaboration. Technical programming difficulties in data entry and calculations were encountered early. Most problems were solved shortly after starting the system. Communication problems from the telephone line and hackers (most common cause of hacking was jamming the website for political reasons - Israeli IP)

occurred occasionally, but were transient. However, this was frustrating to physicians who found they could not always enter data at their convenience. The registry itself was not tampered with and data are backed-up daily by the system. Collaborators had requests, mainly in regards to add or change the diagnosis list. Since the system was flexible to change, requests were discussed and if approved in meetings of the participating physicians, changes were easily implemented. One problem we faced was the classification of the chronic arthritides in childhood. We decided to use juvenile rheumatoid arthritis (JRA), not juvenile idiopathic arthritis (JIA), since the latter classification criteria are still under revision and not yet fully accepted by the international community.

Like other registries, we were dependent on cooperation and collaboration. Some physicians were more meticulous than others in entering their new patients and complete data on each patient. Many physicians did not enter data on referral patterns, drug use and disease progress, therefore these were not analyzed automatically on line. The data we chose to enter was based on the U.S. registry [1]. Currently only physicians enter data. Other personnel can be trained to enter data but this would necessitate additional passwords with limited access for those personnel.

DISCUSSION

Data on nearly 3000 patients were entered into the registry, including >500 with JRA and 100 with SLE. Thus, we have demonstrated the feasibility of establishing a web-based registry in pediatric rheumatology. Israel has several advantages that assisted in the establishment of the registry. All practicing pediatric rheumatologists are part of the Israeli Pediatric Rheumatology Study Group. This group has performed several collaborative studies. Israel has 11 pediatric rheumatologists, which is the highest density per pediatric population in the world (1 per approximately 200,000 children). In Israel, there are pediatric rheumatology clinics in district hospitals as well as tertiary centers and some physicians also have clinics in the community health fund organizations. The clinics are spread throughout the country. Therefore, the vast majority of children with significant rheumatic problems are eventually seen by a pediatric rheumatologist. This

improves the accuracy of incident and prevalence rates that may be derived from the registry as well as the accuracy of the rheumatologic diagnosis.

Since the purpose of this paper was to show the mechanism of the registry we did not analyze in depth patient data. However, similar to other registries, the majority of patients did not have chronic rheumatic conditions [1,2,8,13]. As noted from a previous study, the number of patients with periodic fever syndromes and Behcet's disease was greater than in registries from Western countries due to the greater frequencies of these diseases in the ethnic groups represented in Israel [14].

Future potential uses of registry: The future potential use of the registry depends to a large degree on finding additional funding and collaboration. This tool can be developed into a robust generic tool for pediatric rheumatology that can later be tailored for specific purposes and diseases. This would include more disease related data, outcome measures, and the ability to analyze longitudinal data. Further strengthening of data quality control methods would improve the reliability of the data on the registry. Due to new patient privacy guidelines (especially in countries with legislation) care should be taken in the data entered to web-based systems, and privacy protections and security systems should be strengthened. Automatic reminders to physicians, simplification of data entry and incentives such as authorship on papers and access to data for research purposes will improve compliance. Committees should be formed to decide on the type of data to be entered, definitions of diagnosis and to oversee the operation of the registry.

CONCLUSION

Internet-based registries have the potential to improve data collection and multicenter collaboration. We demonstrated in Israel the feasibility of developing an internet-based registry with limited resources and describe the potential to develop a robust tool in order to advance research efforts in pediatric rheumatology.

REFERENCES

1. Bowyer S, Roettcher P. Pediatric rheumatology clinic populations in the United States: results of a 3 year survey. Pediatric Rheumatology Database Research Group. J Rheumatol 1996;23:1968-74.
2. Malleson PN, Fung MY, Rosenberg AM. The incidence of pediatric rheumatic disease: results from the Canadian Pediatric Rheumatology Association Disease Registry. J Rheumatol 1996;23:1981-7.
3. Symmons DP, Jones M, Osborne J, Sills J, Southwood TR, Woo P. Pediatric Rheumatology in the United Kingdom: data from the British Pediatric Rheumatology Group National Diagnostic Register. J Rheumatol 1996;23:1975-80.
4. Pelkonen PM, Jalanko HJ, Lantto RK, Maleka AL, Pietikainen MA, Savolainen HA, Verronen PM. Incidence of systemic connective tissue diseases in children: a nationwide prospective study in Finland. J Rheumatol 1994;21:2143-6.
5. Kripiarine-Seppanen O, Sarolainen A. Incidence of chronic juvenile rheumatic diseases in Finland during 1980-1990. Clin Exp Rheumatol 1996;14:441-4.
6. Andersson-Gare BA, Fasth A, Andersson J, et al. Incidence and prevalence of juvenile chronic arthritis: a population survey. Ann Rheum Dis 1987;46:277-81.
7. Gare BA, Fasth A. Epidemiology of juvenile chronic arthritis in southwestern Sweden: a 5-year prospective population study. Pediatrics 1992;90:950-8.
8. Denardo BA, Tucker LB, Miller LC, Szer IS, Schaller JG. Demography of a regional pediatric rheumatology patient population. Affiliated Children's Arthritis Centers of New England. J Rheumatol 1994;21:1553-61.
9. Towner SR, Michet CJ Jr, O'Fallon WM, et al. The epidemiology of juvenile arthritis in Rochester, Minnesota, 1960-1979. Arthritis Rheum 1983;26:1208-13.
10. Peterson LS, Mason T, Nelson AM, O'Fallon WM, Gabriel SE. Juvenile rheumatoid arthritis in Rochester, Minnesota 1960-1993: is the epidemiology changing? Arthritis Rheum 1996;39:1385-90.

11. Cassidy JT, Levinson JE, Bass JC, Baum J, Brewer EJ Jr, Fink CW, et al. A study of the classification criteria for a diagnosis of juvenile rheumatoid arthritis. *Arthritis Rheum* 1986;29:274-81.
12. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;25:1271-7.
13. Rosenberg AM. Analysis of a pediatric rheumatology clinic population. *J Rheumatol* 1990;17:827-30.
14. Hashkes PJ. Profile of a pediatric rheumatology practice in Israel. *Clin Exp Rheumatol* 2003;21:123-8.

Table 1: Data collected

Demographic data

Age

Gender

Ethnicity

Geographic region

Disease-related data

Rheumatologic diagnoses

Date of onset

Date of diagnosis

Family history of pediatric rheumatology disease

Referral data

Specialty of referring physician

Health fund organization serving the patient's health needs

Number of prior physicians

If patient was seen by another pediatric rheumatologist

Use of major drugs (including dates started and ended; doses can be entered as an open comment)

Basic outcome data (including dates)

Remission

Relapse

Table 2: Summary Data of Israeli Pediatric Rheumatology Registry (N = 2984)

Age at diagnosis (yrs, mean \pm SD)	9.0 \pm 5.1
Disease duration (months, mean \pm SD)	30.6 \pm 43.0
Time until diagnosis (months, mean \pm SD)	11.5 \pm 29.0
Gender N (%):	Male 1306 (44) Female 1561 (52) Missing data 117 (4)
Ethnicity N (%)	
Jewish - Ashkenazi	702 (24)
Jewish – North African	570 (19)
Jewish – Middle East	266 (9)
Arab – Moslem	470 (14)
Arab – Christian	39 (1)
Druze	54 (2)
Bedouin	25 (1)
Other	37 (1)
Mixed	330 (11)
Missing data	541 (18)
Geographic Distribution N (%)	
Jerusalem and surroundings	698(23)
Tel-Aviv and surroundings	509 (17)
Northern Israel	686 (23)
Central Israel	496 (17)
Southern Israel	190 (6)
Missing data	399 (13)
Other countries	6 (0.2)

Table 3: Partial list of patient diagnoses

Juvenile rheumatoid arthritis		520
Pauciarticular		335
Polyarticular RF-	76	
Polyarticular RF+	15	
Systemic	94	
Uveitis		88
Chronic anterior	44	
Acute anterior		20
Posterior	10	
Unspecified	14	
Other chronic arthritis		107
Psoriatic arthritis	29	
Ankylosing spondylitis	21	
SEA syndrome	37	
Inflammatory bowel disease		16
Sarcoidosis	3	
Reiter's syndrome	1	
Connective tissue diseases		166
SLE	97	
Neonatal lupus	1	
MCTD	3	
Dermatomyositis	23	
Linear scleroderma	25	
Morphea	8	
Systemic sclerosis	4	
Undifferentiated	5	
Vasculitis		206
Kawasaki disease	34	
Behcet disease		50
Polyarteritis nodosa	11	
HSP	82	
Takayasu	2	
Other	27	
Post-Streptococcal arthritis		268
Rheumatic fever	197	
PSRA	71	
Periodic fever syndromes		500
Familial Mediterranean fever		361
PFAPA	95	
Other	22	
Undiagnosed	22	

Non-inflammatory pain syndromes		305
Growing pain	99	
Hypermobility		70
Fibromyalgia	60	
RSD	29	
Anterior patella pain	25	
Psychogenic	7	
Other	15	
Tumors / Malignancies		17
Primary bone malignancy	3	
Leukemia	2	
Osteoid osteoma	4	
Primary bone benign		5
Other	3	

Diagnoses in this table include patients with definite and probable disease. The full list of diagnoses as well as the breakdown into patients with definite and probable disease can be seen at the following LINK: www.moshe-r.net/pedrheumdemo select activity function: national summary data.