

Rheumatic diseases in migrant patients resident in Tuscany: epidemiological data analysis and single-center experience

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SUMMARY

Objective. In the last decades, the number of foreigners in Tuscany has considerably increased with a multiethnic distribution. We reviewed the main rheumatic diseases in the foreign population resident in Tuscany and also reported the experience at the Rheumatology Division of the University Hospital of Careggi, Florence, in order to identify the areas of origin of these patients and the main rheumatic diseases observed in them.

Methods. The collaboration with the Tuscan Region provided data about foreign patients residing in Tuscany on January 1, 2021 (country of origin, chronic diseases). Moreover, we conducted a retrospective review of the clinical charts of our Rheumatologic Division from January 1, 2019, to December 31, 2020.

Results. In Tuscany, on January 1, 2021, there were 61,373 patients with chronic inflammatory rheumatic diseases, and 3994 of them (6.51%) were foreigners. Most patients were born in Europe (39.03%), followed by the Balkans (15%), South America (11.27%), and North Africa (10.31%). Inflammatory joint diseases, Sjögren syndrome, and systemic lupus erythematosus were the most frequent diseases. In the period 2019-2020, 511 foreign patients visited our Rheumatology Division and mainly originated from the Balkans (34.64%), South America (18%), and European countries (16.44%). In these patients, chronic inflammatory joint diseases and connective tissue diseases (systemic sclerosis, Sjögren syndrome, and systemic lupus erythematosus) were the most prevalent diseases.

Conclusions. This study provides a picture of the rheumatic diseases affecting foreign patients residing in Tuscany that are in agreement with the epidemiological data previously provided.

Key words: Migrant patients, rheumatologic diseases, epidemiology, Tuscany.

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■ INTRODUCTION

Rheumatic musculoskeletal disorders (RMDs) seem to be relatively ubiquitous, with the exception of Africa, where these diseases are rarely reported (1). However, the epidemiology of RMDs in the developing world is less known than it is in the developed world, due to limited data (2, 3).

Geoepidemiology (GE) is the study of the distribution of diseases and the determinants of disease gradients in the human population (4). For RMDs, GE investigates the complex combination of genetic predisposition and environmental factors, which is the core of the pathogenesis of autoim-

munity, comparing migrant populations with native populations and with the same ethnic group in their region of origin (1).

In particular, rheumatoid arthritis (RA) has a relatively uniform prevalence (0.5-1%), with the highest frequency in Australia and Jamaica (nearly 2000 cases/100,000 people/year) and the lowest in Sub-Saharan Africa and Caribbean blacks (100 cases/100,000 people/year) (1; 5). The geographic distribution of ankylosing spondylitis (AS) parallels the prevalence of HLA-B27: populations with a high percentage of HLA-B27 carriers, such as North American Pima Indians, Alaskan Eskimos, and Northern Norway Laps, have the highest disease frequencies (4500 cases/100,000 people/year for the

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first, 1100-1400 cases/100,000 people/year for the others), while Americans and Europeans have similar disease prevalence, and Japanese people demonstrate the lowest AS frequency (<1 case/100,000 people/year). Among connective tissue diseases (CTDs), systemic sclerosis (SSc) has a higher frequency in the USA and Australia, while in Europe a general north-south gradient is evident, with a greater number of cases in Greece and France as compared with Northern Europe (Great Britain and Iceland) (6). Systemic lupus erythematosus (SLE) has a homogeneous distribution, with the exception of some regions of Africa, where its rate is low, and Brazil, where its rate is relatively high (1).

In the last few decades, the number of foreigners residing in Tuscany has considerably increased. In Italy, Tuscany is the region with the highest number of foreigners and multiethnic immigration rate, with 173 nations represented. More than half of the foreigners residing in Tuscany come from central-eastern Europe, followed by Asia (mainly from China, but with a consistent presence also from the Philippines, Sri Lanka, India, Bangladesh, and Pakistan), Africa (Morocco between the states of North Africa and Senegal for the central-southern area), and less frequently from America (Peru, Brazil, the Dominican Republic, Ecuador, and Cuba) (7).

In this paper, we reviewed the frequencies of the main RMDs in the foreign population resident in Tuscany, with a focus on the foreign patients that accessed the Rheumatology Division of the University Hospital of Careggi, Florence, in the period 2019-2020. The project aimed to analyze the Tuscan population of foreign patients who accessed specialized rheumatologic hospitals in the region in order to identify the areas of origin of these patients and the rheumatic diseases from which they are affected.

■ MATERIALS AND METHODS

The study was carried out in collaboration with *Azienda Regionale di Sanità* (ARS). It is a technical body of the Tuscan Region that carries out consultancy and research

activities aimed at institutions, individuals, and organizations operating in the regional health and social system, as well as a variety of interested parties.

ARS has provided the following data (personal communication), extracted on January 1, 2021:

- 1) number of foreign patients residing in Tuscany, divided by country of origin, that suffer from a chronic inflammatory rheumatic disease;
- 2) frequency of the main chronic inflammatory rheumatic diseases that affected these patients.

The data relating to rheumatological diseases were obtained from the database of exemption codes from copays. Therefore, it was not possible to include in our research those pathologies for which this code is not foreseen, such as fibromyalgia, osteoarthritis (OA), osteoporosis, gout, and other microcrystal diseases.

We grouped the various countries of origin in macro-areas, mainly corresponding to continents, also subdivided into the north, central, and south parts, with some exceptions. With the term "Europe" we considered all the European continent except for the Balkan region. This area was considered separately due to the large number of patients we found in our sample, in order to evidence them. We also separated Russia due to its belonging to two continents, Europe and Asia.

Then, we conducted a retrospective review of the clinical charts of RMD patients followed in the Rheumatology Division of the University Hospital of Careggi, Florence, from January 1, 2019, to December 31, 2020, and we selected all the patients who were born outside Italy.

For all the foreign patients we collected the following data: date of birth, country of birth, sex, diagnosis of rheumatic disease (if present).

The continuous variables are presented as mean \pm standard deviation, while categorical variables are presented as absolute frequency and percentage of each category.

Patients who had missing data regarding their country of origin or rheumatological disease were excluded from the analysis.

■ RESULTS

Population description

The foreigners resident in Tuscany on January 1, 2021, were 793,838. The data extracted by ARS (personal communication) at the same time point showed a total of 61,373 patients with chronic inflammatory rheumatic diseases: 57,355 (93.45%) were born in Italy and 3994 (6.51%) were foreign patients, 0.05% of the total foreign population. For 24 patients (0.04%) the country of birth could not be obtained so they were excluded from the subsequent analysis.

In Table I the distribution of the various countries of origin of these patients is reported (number of patients and percentage of the total) (data from ARS, personal communication).

The majority of patients were born in the European Union (1559 patients, 39.09%),

mainly in Romania (554 patients, 38.13%), France (157 patients, 10.80%), Poland (145 patients, 9.98%), Germany (135 patients, 9.29%) and Switzerland (117 patients, 8.05%).

The second most represented area is the Balkan region (599 patients, 15%), followed by South America (450 patients, 11.27%), mainly Peru and Brazil, Asia (422 patients, 10.56%), North Africa (412 patients, 10.31%), with the great majority of patients coming from Morocco (238 patients, 57.77%). Only a few patients were born in Oceania, Russia, South Africa, Caucasus, and Southeast Asia.

Rheumatic diseases in foreigners resident in Tuscany

Table II shows the broad spectrum of rheumatic diseases (number and percentage) in Italian and foreign patients: 29,646 Italian patients and 2590 foreign patients with a

Table I - Distribution of the various countries of birth of patients with chronic inflammatory rheumatic diseases in Tuscany on January 1, 2021 (data from *Azienda Regionale di Sanità*, personal communication).

Country of birth	n (%)	Country of birth	n (%)
Total	61.373 (100)		
Italy	57.355 (93.45)		
Country other than Italy	3.994 (6.51)		
Europe	1.559 (39.03)	Middle East	52 (1.30)
France	157 (10.07)	Iran	25 (48.08)
Germany	135 (8.66)	Turkey	8 (15.38)
United Kingdom	106 (6.80)	Other countries	19 (36.54)
Poland	145 (9.30)	North Africa	412 (10.31)
Romania	554 (35.54)	Libya	81 (19.66)
Switzerland	117 (7.50)	Morocco	238 (57.77)
Ukraine	97 (6.22)	Tunisia	46 (11.16)
Other countries	248 (15.91)	Other countries	47 (11.41)
Asia	422 (10.56)	North America	78 (1.95)
China	120 (28.44)	Canada	18 (23.08)
Philippines	86 (20.38)	U.S.A.	60 (76.92)
India	71 (16.82)	Oceania	21 (0.52)
Pakistan	48 (11.37)	Australia	19 (90.48)
Sri Lanka	58 (13.74)	Other countries	2 (9.52)
Other countries	39 (9.24)	Russia	38 (0.95)
Balkans	599 (15.00)	South Africa	23 (0.57)
Albania	447 (74.62)	Cape Verde	6 (26.09)

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Country of birth	n (%)	Country of birth	n (%)
Moldova	58 (9.68)	Republic of South Africa	6 (26.09)
Serbia	43 (7.18)	Other countries	11 (47.82)
Other countries	51 (8.52)	South America	450 (11.27)
Caucasus	16 (0.40)	Argentina	54 (12.00)
Central Africa	180 (4.51)	Brazil	98 (21.78)
Ethiopia	31 (17.22)	Colombia	44 (9.78)
Nigeria	20 (11.11)	Peru	147 (32.67)
Senegal	73 (40.56)	Venezuela	38 (8.44)
Other countries	56 (31.11)	Other countries	69 (15.33)
Central America	103 (2.58)	Southeast Asia	35 (0.88)
Cuba	25 (24.27)	Other countries	6 (0.15)
Dominican Republic	55 (53.40)	Unknown	24 (0.04)
Other countries	23 (22.33)		

rheumatologic disease were found (data from ARS, personal communication). As expected, the most frequent diseases were chronic inflammatory joint diseases [RA, psoriatic arthritis (PsA), AS], Sjögren syn-

drome (SS), and SLE, with a similar distribution in both groups. The diseases that have a higher percentage of foreign patients out of the total are RA, AS, SLE, polymyositis, and Takayasu arteritis.

Table II - Rheumatologic diseases in Italian and foreign patients resident in Tuscany on January 1, 2021 (data from Azienda Regionale di Sanità, personal communication).

Diseases	n (%)		% foreigners over total
	Foreign patients	Italian patients	
Rheumatoid arthritis	914 (35.29)	8.599 (29.00)	9.65
Psoriatic arthritis	377 (14.55)	6.968 (23.50)	5.13
Ankylosing spondylitis	353 (13.63)	2.601 (8.77)	11.95
Sjögren syndrome	297 (11.47)	4.341 (14.64)	6.40
Systemic lupus erythematosus	266 (10.27)	1.915 (6.46)	12.20
Other connective tissue diseases	195 (7.53)	2.455 (8.28)	7.36
Juvenile rheumatoid arthritis	61 (2.35)	874 (2.94)	6.52
Systemic sclerosis	42 (1.62)	560 (1.89)	6.98
Behcet disease	26 (1.00)	254 (0.86)	9.28
Polymyositis	13 (0.50)	114 (0.38)	10.24
Giant cells arteritis	8 (0.31)	208 (0.70)	3.70
Dermatomyositis	7 (0.27)	128 (0.43)	5.18
Granulomatosis with polyangiitis	7 (0.27)	158 (0.53)	4.24
Takayasu arteritis	6 (0.23)	36 (0.12)	14.28
Felty syndrome	2 (0.08)	81 (0.27)	2.41
Panarteritis nodosa	1 (0.04)	44 (0.15)	2.22
Other diseases	15 (0.58)	310 (1.05)	4.61
Total	2.590	29.646	8.03

The data relating to the geographical origin and the rheumatic diseases detected were then cross-referenced (Figures 1 and 2) (data from ARS, personal communication).

In Figure 1, the relative frequencies of rheumatic diseases in the different groups of geographical origin are reported. It is evident that in all geographical groups, chronic inflammatory joint diseases, SS, and SLE are the most represented diseases. In people coming from the Middle East and North Africa, we also found many cases of Behcet's disease, consistent with the literature data (7). In South African patients, we observed a great prevalence of RA, while the other diseases were very rare.

In Figure 2, the relative frequencies of the geographical origins for each rheumatologic condition are reported. The European Union, Asia, the Balkans, and South America are the most represented for almost all diseases. For Behcet's disease and polymyositis, a great proportion of patients were

from North Africa, even if the numbers were small. Surprisingly, none of the patients with Takayasu arteritis came from Asia, unlike what we could have expected due to the epidemiology of the disease.

Rheumatic diseases in foreigners followed at the Rheumatology Division of the University Hospital of Careggi

In the second part of the study, we studied the cohort of foreign patients who were referred to our outpatient clinic.

In the period 2019-2020, 511 foreign patients (born in a country other than Italy) were visited: 434 were women (84.93%) and 77 men (15.07%), with an average age of 52 ± 13 years (18-87 years).

These patients underwent a total of 1,406 visits (639 in 2019 and 767 in 2020). In 2020, due to COVID-19 pandemic, in our center the outpatient activity was suspended from March to June; as a consequence, some of the visits (182 visits, 23.73% of the total) were carried out in telemedicine/ teleconsult-

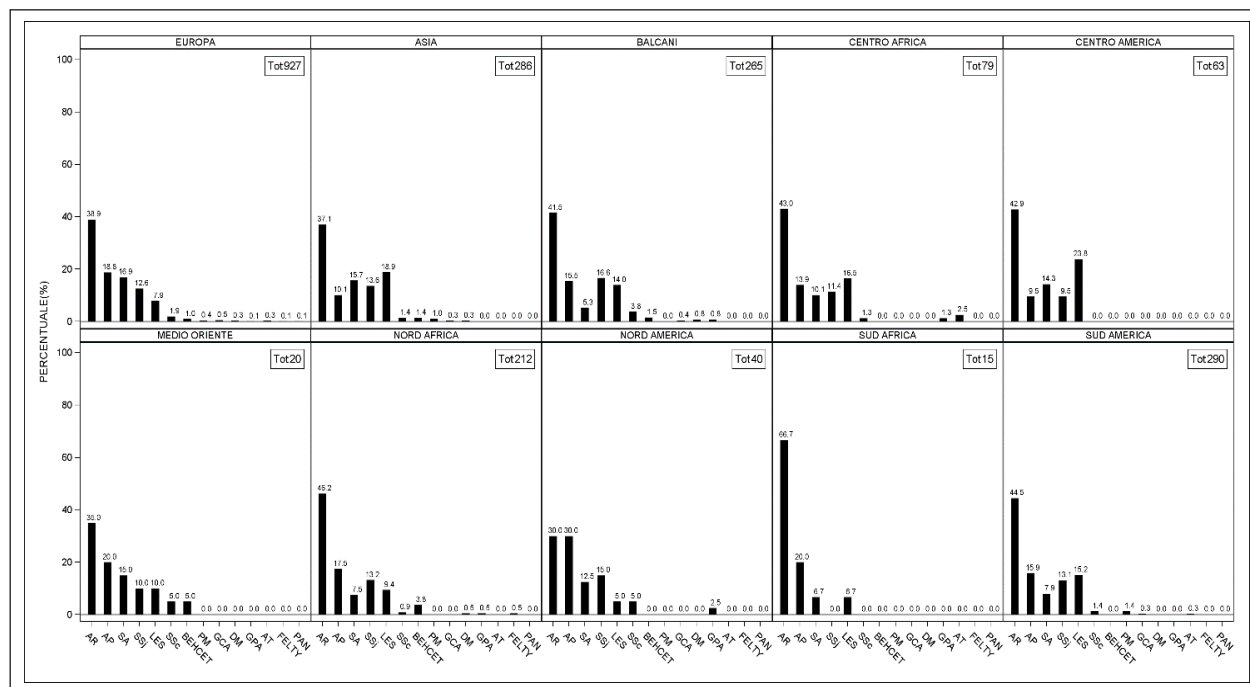


Figure 1 - Relative frequencies of rheumatologic diseases in the different groups of geographical origin in foreign patients resident in Tuscany on January 1, 2021 (data from Azienda Regionale di Sanità, personal communication).

RA, rheumatoid arthritis; PsA, psoriatic arthritis; AS, ankylosing spondylitis; SS, Sjögren syndrome; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; BEHCET, Behcet disease; PM, polymyositis; GCA, giant cells arteritis; DM, dermatomyositis; GPA, granulomatosis with Polyangiitis; TA, Takayasu arteritis; FELTY, Felty syndrome; PAN, panarteritis nodosa.

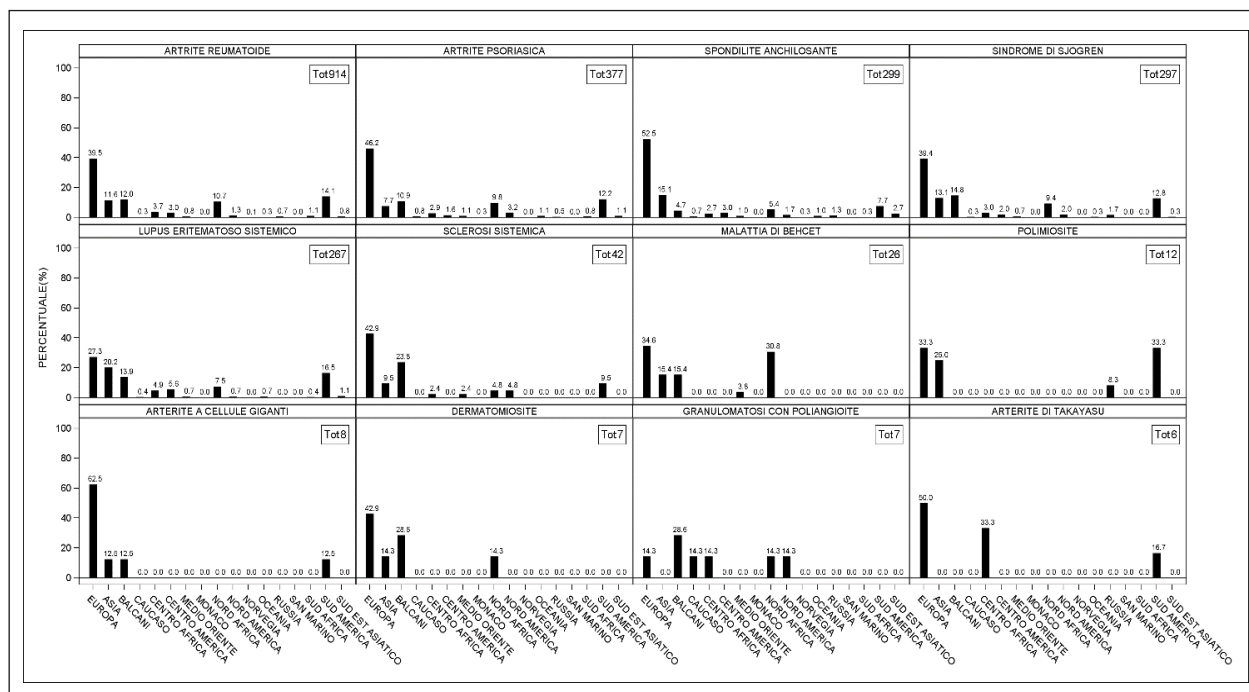


Figure 2 - Relative frequencies of the geographical origins for each rheumatologic disease in foreign patients resident in Tuscany on January 1, 2021 (data from Azienda Regionale di Sanità, personal communication).

tation mode, while 585 visits (76.27%) were carried out in the traditional way. Considering the geographic origin of these patients, most of them were born in Balkan countries (177 patients, 34.64%), in particular in Romania (15.66%) and Albania (13.89%), in South America (92 patients, 18%), with over half of the patients coming from Peru (55.44%), in the European Union (84 patients, 16.44%), mainly from Poland (32.14%), and France (10.72%). Considering eastern countries, patients from Ukraine (13.10%) were also found. Less than 10% of patients were born in Asia (9.78%) and North Africa (8.41%), while few patients came from North and Central America, the Middle East, and Central and South Africa (respectively 3.72%, 2.35%, and 3.53%). In most cases, the patients were affected by chronic inflammatory joint diseases, such as RA (137 patients, 26.81%), PsA (29 patients, 5.67%), or AS (40 patients, 7.83%). CTDs were also very frequent, in particular, SSc (36 patients, 7.04%), SS (22 patients, 4.30%), and SLE (11 patients, 2.15%), as well as OA (47 patients, 9.20%). For 114

patients, the diagnosis was not known, either because it is still being defined or because the patient was lost before a diagnosis was ascertained. We then analyzed the disease distribution by geographical area of origin (Table III): RA was evenly distributed and most represented in Asia, Balkan countries, North Africa, and South America. A great prevalence of SSc was observed in Balkanic patients, almost as frequent as in European countries. The number of patients with PsA was exiguous and for this reason, these patients were included in the group “other”.

DISCUSSION AND CONCLUSIONS

The first part of this study analyzes the distribution of chronic rheumatological diseases in foreign subjects residing in the Tuscan region. According to what emerges from our analysis, there are almost 4000 foreign resident patients who, on January 1, 2021, suffered from a rheumatological disease. These patients have benefited from specialist

outpatient visits and laboratory and instrumental examinations at the public health facilities in Tuscany. Therefore, it is important to monitor them from an epidemiological, socio-sanitary, and economic point of view. In this group of foreigners, almost all the rheumatic diseases are represented except for those that are not officially recognized (meaning the diseases for which the attribution of an exemption code is not foreseen), and therefore they cannot be detected by ARS, such as fibromyalgia, osteoporosis, or OA. The frequency of the rheumatic diseases was similar in the various ethnic groups, with chronic inflammatory joint

diseases (RA, PsA, AS) and common CTDs (SS, SLE, and SSc) most represented.

If compared with the prevalence of rheumatological diseases in Europe or in Italy, the numbers appear to be lower. This is most likely due to the presence of a large number of undiagnosed diseases, related to the difficulty of accessing treatment for linguistic problems and poor compliance; these patients often had an initial evaluation at symptoms' onset or in an acute phase without continuing the follow-up and investigations that would allow the formulation of a diagnosis. Furthermore, as reported above, this analysis excludes all those conditions

Table III - Distribution of the diseases by the geographical area of origin, in foreign patients visited at the Rheumatology Department of the University Hospital of Careggi, Florence, from January 1, 2019, to December 31, 2020, absolute number and row percentage.

	Diseases										
	RA	AS	SSc	SLE	SS	RAY	FIBRO	OA	OTHER	UNK	TOT
Europe	19 (22.62%)	5 (5.95%)	9 (10.71%)	2 (2.38%)	3 (3.57%)	5 (5.95%)	2 (2.38%)	9 (10.71%)	17 (20.24%)	13 (15.48%)	84
Asia	16 (32.00%)	3 (6.00%)	1 (2.00%)	2 (4.00%)	1 (2.00%)	0	0	1 (2.00%)	17 (34.00%)	9 (18.00%)	50
Balkans	31 (17.51%)	15 (8.47%)	20 (11.30%)	2 (1.13%)	11 (6.21%)	7 (3.95%)	7 (3.95%)	18 (10.17%)	19 (10.73%)	47 (26.55%)	177
Caucasus	0	0	0	0	0	0	0	1 (25.00%)	1 (25.00%)	2 (50.00%)	4
Central Africa	5 (33.33%)	0	0	0	0	1 (6.67%)	0	1 (6.67%)	2 (13.33%)	6 (40.00%)	15
Central America	2 (40.00%)	0	0	1 (20.00%)	0	0	0	0	2 (40.00%)	0	5
Middle East	3 (25.00%)	2 (16.67%)	3 (25.00%)	1 (8.33%)	0	0	1 (8.33%)	1 (8.33%)	0	1 (8.33%)	12
North Africa	15 (34.88%)	7 (16.28%)	1 (2.33%)	1 (2.33%)	2 (4.65%)	0	1 (2.33%)	3 (6.98%)	5 (11.63%)	8 (18.60%)	43
North America	4 (28.57%)	1 (7.14%)	0	0	1 (7.14%)	0	1 (7.14%)	3 (21.43%)	2 (14.29%)	2 (14.29%)	14
Russia	3 (30.00%)	1 (10.00%)	0	1 (10.00%)	1 (10.00%)	0	0	1 (10.00%)	0	3 (30.00%)	10
South Africa	2 (100.00%)	0	0	0	0	0	0	0	0	0	2
South America	37 (40.22%)	5 (5.43%)	1 (1.09%)	1 (1.09%)	3 (3.26%)	1 (1.09%)	5 (5.43%)	9 (9.78%)	8 (8.69%)	22 (23.91%)	92
Southeast Asia	0	1 (33.33%)	1 (33.33%)	0	0	0	0	0	0	1 (33.33%)	3
Total	137 (26.81%)	40 (7.83%)	36 (7.04%)	11 (2.15%)	22 (4.30%)	14 (2.74%)	17 (3.33%)	47 (9.20%)	73 (14.29%)	114 (22.31%)	511

RA, rheumatoid arthritis; AS, ankylosing spondylitis; SSc, systemic sclerosis; SLE, systemic lupus erythematosus; SS, Sjögren syndrome; RAY, Raynaud phenomenon; FIBRO, fibromyalgia; OA, osteoarthritis; UNK, unknown.

for which there is no official recognition, and which are therefore not detectable by the ARS database.

Comparing the frequencies of rheumatological diseases in subjects born in Italy with those born in foreign countries, the most represented disease was RA, as expected from the prevalence data in the literature (1, 5). Differences are noted instead with some CTDs, such as SLE, which was particularly frequent in foreigners, a fact that is difficult to interpret in light of the known literature that sees this condition as rare in African countries (1), which are the birthplace of approximately 15% of our foreign population. As regards the remaining diseases, the distribution between subjects born in Italy and foreigners was quite homogeneous.

Our results confirm some epidemiological data from the literature. For example, we found a large proportion of patients with Behcet's disease derived from North Africa, the Middle East, and Asia. This is in line with the distribution of this disease in the countries along the Silk Road (8). Conversely, we found no patients with Takayasu arteritis from Asia or other Eastern countries, even if it is traditionally considered more frequent in young Asian women (9). This is despite the fact that Asian subjects represented approximately 10% of our Tuscan sample.

The analysis of the data from our Rheumatologic Department shows a disease distribution in foreign patients that was similar throughout the entire region. Among the various diseases, we could also detect a small number of patients who were suffering from fibromyalgia, OA, and Raynaud's phenomenon. A slight inconsistency was observed for the Asian population. It should be noted that only 50 Asian patients were visited at the Rheumatologic Department of the University Hospital of Careggi; among them, only 16 were Chinese. It is a very small number if compared to the large Asian population resident in Tuscany and to the data provided by ARS (personal communication). The reasons are not easily determined; the difficulties in linguistic integration probably play a role, making it hard for patients to access healthcare facilities;

another possible explanation concerns cultural reasons and a certain reticence of Asian patients to manifest health problems. This study shows that in Tuscany, the migratory population derived from different parts of Europe, North Africa, Asia, and South America is affected by numerous rheumatic diseases. The number of patients appears substantially in line with what is known from epidemiological data, with some variations, probably linked to the small number of patients analyzed.

The main limitations of our study concern, as already discussed, the possibility of analyzing only pathologies for which there is official recognition, excluding from our observation a vast range of conditions that are widespread and disabling for the population, such as OA or fibromyalgia. Furthermore, we have no information on the patients analyzed except for the country of birth and the disease. Therefore, within the population defined as "foreign", there is a heterogeneity of conditions, from patients who were born in countries other than Italy but moved there in childhood to those who only arrived in adulthood. This therefore does not allow us to consider the environmental factors that can influence the development of rheumatological pathologies and their distribution in this group of subjects. Regarding the analysis of the Rheumatology Clinic sample, the main limitation is certainly the presence of a small sample of patients due to the short observation period.

Contributions

LC, MMC, designed the study; LC, PF, BB, LT, FV, collected the data and did the data analysis; LC, drafted the initial manuscript. All authors reviewed and revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflict of interest

The authors declare no potential conflict of interest.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

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Availability of data and materials

Data and materials are available from the corresponding author.

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