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Review Article / Преглед литературе

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Prevalence of spondyloarthritis and its subtypes – are they really comparable?

Преваленција спондилоартритиса и његових подтипова – да ли је заиста упоредива?

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SUMMARY

Introduction/Objective Increasing spondyloarthritis (SpA) prevalence in the last several decades cannot be attributed to disease manifestations alone.

Review of the prevalence of SpA and the subtypes: ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), SpA related to inflammatory bowel disease (IBD) and undifferentiated SpA (UnSpA).

Methods Literature search of MEDLINE via PubMed, Google Scholar and Embase databases using terms for spondyloarthritis, and prevalence, with an additional hand search.

Results As compared with southern European countries, northern European countries (Scotland, Sweden, France) showed lower SpA prevalence rates (0.21-0.45% vs 1.06% and 1.35% in Italy and Turkey, respectively). The lowest world SpA prevalence was in African and Southeast Asian countries (0.00-0.19%), and the highest was in Alaska (2.5%). The widest variability in PsA prevalence was in Europe (northern 0.02-0.19%, southern 0.42%). The lowest world PsA prevalence was in Japan (0.001%), followed by China (0.01-0.10%). The European ReA prevalence ranged from 0.04% in Greece to 0.10% in Serbia and Germany and the European UnSpA prevalence varied from 0.02% in Serbia to 0.67% in Germany; the highest world UnSpA prevalence was in Lebanon (3.40%). Studies aimed at estimating the SpA prevalence differed in sampling strategy and confirmation criteria, different cut-offs for age groups inclusion, presentation of standardized or row results, etc.

Conclusion Variation in the SpA prevalence cannot be attributed to genetic or geographic distribution only. Differences in methodology of studies add to the diversification, described more in-depth in this manuscript.

Keywords: epidemiology; prevalence; spondyloarthritis; ankylosing spondylitis; psoriatic arthritis

САЖЕТАК

Увод/Циљ Пораст преваленције спондилоартритиса у последњих неколико деценија не може се приписати само манифестацијама болести.

: Преглед преваленције спондилоартритиса (СпА) и његових подтипова : анкилозирајућег спондилитиса (АС), псоријазног артритиса (ПсА), реактивног артритиса (РеА), СпА повезаног са инфламаторним болестима црева и недиферентованог СпА (НеСпА), са специјалним освртом на методолошке разлике и географске варијације.

Методе Учињено је претраживање литературе са *PubMed, Google Scholar* и *Embase* база података уз додатно ручно претраживање у односу на термин спондилоартритис и његових подтипова у комбинацији са преваленцијом.

Резултати Земље северне Европе (Шкотска, Шведска, Француска) имају ниже стопе преваленције СпА (0.21%-0.45%) у поређењу са јужним (Италија-1.06% и Турска-1.35%). Најнижа преваленција СпА у свету забележена је у Афричким и југоисточним Азијским земљама (0.00%-0.19%), а највиша на Аљасци (2.5%). Највећа варијабилност у преваленцији ПсА запажена је у Европи (северни део 0.02-0.19%, јужни 0.42%). Најнижа преваленција ПсА у свету забележена је у Јапану-0.001%, затим у Кини 0.01-0.10%. У Европи се преваленција РеА креће од 0.04% у Грчкој до 0.10% у Србији и Немачкој, док је преваленција УнСпА од 0.02% у Србији до 0.67% у Немачкој. Највиша преваленција УнСпА у свету нађена је у Либану-3.40%. Студије које одређују преваленцију СпА разликују се у бројним карактеристикама: различит метод формирања узорака и употребљених критеријума, укључивање различитих старосних група, различит приказ резултата итд.

Закључак Варијације у преваленцији СпА не могу се приписати само генетским или географским разликама. Различита преваленција делимично је условљена и неуједначеним методама истраживања, детаљније описаним у овом чланку.

Кључне речи: епидемиологија; преваленција; спондилоартритис; анкилозирајући спондилитис; псоријазни артритис

INTRODUCTION

Spondyloarthritis (SpA) comprises ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), SpA related to inflammatory bowel diseases (IBD) such as Crohn`s disease or ulcerative colitis, and undifferentiated SpA (UnSpA). Common SpA clinical features are spinal, sacroiliac and peripheral joint inflammation, enthesitis or some extra-articular manifestations (uveitis, skin or mucosal changes, cardiovascular or pulmonary changes).

SpA prevalence estimates range widely both in developed and developing countries, from 0.03% in the APLAR region (New Zealand in Oceania to Jordan in the Middle East) to 2.5% in Russian and Alaskan Eskimos [1, 2, 3] (Figure 1). Particularly, African black race populations have shown virtually non-existent SpA prevalence, as in Sub-Saharan Africa, Zimbabwe and Nigeria [4,5].

Differences in the prevalence of SpA and its subtypes, apart from geographic, racial and cultural influences, could also be due to differences in the methodology used in studies (various sampling and case identification strategy with different classification criteria, diverse age groups included, presentation of row or standardized results, etc.). For example, in the last decades, PsA has been identified by a number of different criteria [6,7].

This study aimed to review the estimates of prevalence of SpA and its subtypes: AS, PsA, ReA, IBD SpA and UnSpA, specifically emphasizing differences in methodology and variations in geography.

METHODS

Review involved a search of the literature in MEDLINE via PubMed, Google Scholar and Embase databases with the terms spondyloarthritis, spondyloarthropathy, ankylosing spondylitis, psoriatic arthritis, reactive arthritis, inflammatory bowel disease spondyloarthritis, undifferentiated spondyloarthritis and prevalence, with an additional hand search. A total of 15325 titles and abstracts were reviewed; the full text of 292 articles was read thoroughly; and data for 67 reports are presented and compared here.

SPONDYLOARTHRITIS PREVALENCE

The Asian SpA prevalence ranged from 0.03% in Manila to 1.05%- 1.3% in Turkey [1,8-13]. The SpA standardized prevalence in the whole APLAR region was 0.19% (Davatachi et al)[1]. The SpA prevalence in Europe ranged from 0.21% in Scotland to 1.9% in Germany [14-23]. In Serbia, it was 0.32% [17] (Table 1). The estimated SpA prevalence in the United States was 0.35% to 1.31%

[24,25]. The Australian urban SpA prevalence was 0.21%, but was 0.50% in Australian Aboriginals [1].

Comparison of the world SpA prevalence was limited by methodology discrepancies: various sample sizes, different age limitations (15, 16, 18, 20 years), and different presentation of the achieved results (row or standardized) (Table 1). However, the prevalence was lower in tropical zone countries (Africa or South Asia and Southeastern Asia [Phillipines, Pakistan, Malasya, Thailand, China]) [2,7-10] than in northern countries, with the highest rate in Alaska [4] (Graph 1). On the contrary, prevalence was lower in northern Europe (Scotland, Sweden, France) [14,18,16] than southern Europe (Italy and Turkey) [21,12,13] (Figure 1), which contrasted with the reported rheumatoid arthritis prevalence [26]. Inequalities in methodologies of SpA studies are described in Table 1.

ANKYLOSING SPONDYLITIS PREVALENCE

A wide range of AS prevalence was reported as well (Table 2, Figure 2). The highest AS prevalence was found in Canadian Indigenous Haida Indians, 6.0% [27]. However, no AS cases were found in African countries: Zimbabwe, Nigeria and Togo [28-30]. For Southeast Asian and Pacific regions, AS prevalence estimates ranged from 0.01% in Japan to 0.49% in Turkey [31-33,12] (Table 2). The European AS prevalence ranged from 0.08% in France and Serbia [15,17] to 0.86% in Germany [23] [34,18,21,22,35-38] and was 1.1% to 1.4% in Norway [39, 40] (Table 2, Figure 2). The AS population prevalence in the United States was estimated at 0.35% and 0.52% [24,25] (e.g., 0.13% for the white race only [41]). The Alaskan Eskimo AS prevalence was 0.40% [3].

AS prevalence estimates were lower in African [28-30] and South and Southeast Asian countries [31-33] than in northern Europe and the United States [40, 25, 27] (Figure 2). Differences in the studies are further evaluated in Table 2.

PSORIATIC ARTHRITIS PREVALENCE

The widest variability in SpA prevalence was for PsA and was highest in Europe: 0.42% in Italy [21] (Figure 3). As one of the SpA-related diseases, PsA was not found in certain African countries either (in accordance with the virtual non-existence of SpA), and the non-existence of PsA was confirmed by studies from Uganda and Sub-Saharan Africa [42,29]. PsA prevalence was low in Southeast Asia and Pacific regions as well — 0.001% in Japan and 0.10% in China [43, 44]. Europe had the widest PsA prevalence range, lower in the northern than southern part, ranging from 0.02% in Sweden to 0.42% in Italy [17,45-48,34,15,23,49,36,37,50,21] (Figure 3, Table 3). The prevalence was

0.09% in Serbia. The prevalence ranged from 0.07% to 0.25% in the United States [41,51] and was 0.12% in Minnesota [52] and 0.10% in Alaskan Eskimos [3]. The prevalence in South America was 0.07% [53].

Differences in PsA prevalence studies are described in more detail in Table 3.

REACTIVE ARTHRITIS PREVALENCE

Results of the ReA prevalence estimation studies cannot be generalized because of periodic and geographic variations in "disease trigger factors," such as *Salmonella, Shigella, Yersinia and Campylobacter* bacteria species as well as *Chlamydia* and *Mycoplasma* subspecies. In fact, only a few ReA prevalence studies were performed, mostly under the SpA disease prevalence estimation. The ReA prevalence was 0.04% in Greece [19], 0.09% in Italy [21] and 0.10% in Serbia and Germany [17, 23].

INFLAMMATORY BOWEL DISEASE SPONDYLOARTHRITIS PREVALENCE

The prevalence of IBD SpA (Crohn`s disease or ulcerative colitis) has not been studied much and was less frequently reported than IBDs themselves. According to the few reported studies, the IBD SpA prevalence ranged from 0.01% in Sweden (18] to 0.03% in Serbia [17], 0.04% in Greece [19] and 0.09% in Italy [21]. It was 0.05% to 0.25% in the United States [25].

Prevalence related to IBD type was evaluated by one US study [41]: the prevalence of ulcerative colitis SpA was 0.03% and Crohn`s disease 0.01%. Karreman et al. [54] found an SpA prevalence of 13% in IBD patients, with the pooled prevalence for AS of 3%, peripheral arthritis 13% and sacroiliitis 10%.

UNDIFFERENTIATED SPONDYLOARTHRITIS PREVALENCE

The UnSpA impact and clinical manifestations are not fully understood. In general, UnSpA should be considered in patients presenting inflammatory back pain or peripheral joint arthritis, enthesopathy or alternative buttock pain, not accompanied by some SpA-disease specific features such as spondylitis, psoriasis, Crohn s disease, ulcerative colitis, proven previous urogenital or gastrointestinal infection.

The highest UnSpA prevalence was in Lebanon, 3.4% [55]. In Asia, the representative China had a 0.24% prevalence [56]. In Europe, the UnSpA prevalence estimate for Serbia was 0.02% [17]; Greece, 0.03% [19]; France, 0.04% [15]; Sweden, 0.10% [18]; and Germany, 0.67% [23]. The UnSpA prevalence in the United States was 0.37% [25] and in Alaskan Eskimos 1.30% [3,57].

DISCUSSION

Although historically considered sporadic cases of rheumatoid arthritis and reported at the beginning as "rheumatoid spondylitis" or "seronegative variants of RA," AS and PsA have over time been shown as not only separate diseases but also diseases of constantly growing impact and importance. When the SpA concept was promoted for several seronegative diseases characterized by certain common features, thereby enabling different diseases to be classified into a unified diagnosis a few decades ago, they might be classified as SpA.

SpA prevalence has increased in the past decades. With the universal health system in France, the AS prevalence was estimated at 0.005% in 1994 [58], 0.08% in 2001 (French population study) [15] and 0.43% in 2015 (French population-based study) [16].

European 21st century studies showed high SpA prevalence as well: Sweden 0.45%, France 0.43%, Greece 0.49%, Lithuania 0.84%, Turkey 1.05%, Italy 1.06% and Portugal 1.6%. The last-century SpA prevalence even exceeded that for rheumatoid arthritis (as one of the most prevalent inflammatory rheumatic diseases [59]) in Japan, Germany, Turkey, Lithuania, China, Italy, Australian aboriginals and the United States but was similar to the rheumatoid arthritis prevalence in France and Serbia [17]. This fact could be explained by a better understanding of the SpA concept both by patients and physicians as well as by introducing new classification criteria, the ESSG [60]. The newest ASAS classification criteria [61] were used by several studies, reporting high SpA prevalence estimates as well: 0.43% in France (0.36% for axial SpA and 0.12% for peripheral SpA) [16], 1.35% in Turkey [13] and 0.70% for axial SpA alone in the United States [24].

The first study of the prevalence of pooled SpA and its subtypes was performed in 2016 by Stolwijk et al. The general population pooled prevalence of SpA ranged from 0.20% in Southeast Asia to 1.61% in northern Arctic communities; the AS prevalence ranged from 0.02% in Sub-Saharan Africa to 0.35% in northern Arctic communities; and the PsA prevalence ranged from 0.01% in the Middle East to 0.19% in Europe [62]. However, only a few studies from this meta-analysis were truly representative of the general population, for a high risk of bias [62] besides other methodological variations described more in depth in the article.

The limitation of our review is that we could not track the human leukocyte antigen B27 (HLA-B27) prevalence in all studies included and connect its range with prevalence differences. According to the DESIR cohort, diagnostic delays are less in HLA-B27–positive than –negative patients [63]. High HLA-B27 prevalence is generally positively correlated with SpA prevalence, especially axial SpA [64]. Our review found the highest SpA prevalence in Alaskan Eskimos, 2.5% [3], of whom 25% to 40% are HLA-B27–positive [64]. In the current review, second-place SpA prevalence was found in Russian Chukotka Eskimos, 2.5%, with HLA-B27 prevalence at 34%. The highest AS prevalence (6%) was found in Haida Indians living in the Queen Charlotte Islands of Canada [27], of whom 50% are HLA-B27–positive. However, although the HLA-B27 prevalence varies from 10% to 16% in northern European countries [64], the latest studies have shown an AS prevalence of 0.12% in Sweden, 0.15% in Finland and 0.26% in Norway [18, 35, 39].

In conclusion, although the wide SpA prevalence in different geographic regions could be attributed in part to HLA-B27 positivity, other factors may also play a role, such as geographic differences [59]. In addition, prevalence variations could be only partially due to genetic or environmental factors or geographic distribution [65] and are certainly affected by differences in case definition and case confirmation strategies as well as by other variations in applied methodologies [66].

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Table 1. Spondyloarthritis prevalence

Reference	Country	Year	Age	Population, area, No of participants	Criteria	Prevalence (%) Men	Women	All
EUROPE								
Steven (14)	Scotland	1992	15+	Mixed, Scotish islands	Doctor dg			0.21*
Saraux (15)	France	2001	18+	Mixed, France 9395	Doctor dg	0.31	0.29	0.30*
Constantino (16)		2010	35+	Gazel Cohort, 18757	ASAS			0.43*
Zlatkovic-Svenda (17)	Serbia	2008	18+	Mixed, Serbia 6213	Doctor dg	0.34	0.31	0.32*
Haglund (18)	Sweden	2011	15+	Mixed, south Sweden	Register[p]			0.45
Trontzas (19)	Greece	2005	19+	Mixed, 7 areas, 10647	ESSG			0.49*
Adomaviciute (20)	Lithuania	2008	18+	Urban, Lithuania, 6542	Doctor dg	1.36	1.34	0.84*
De Angelis (21)	Italy	2007	18+	Mixed, Marche, 3664	ESSG			1.06
Bruges-Armas (22)	Portugal	2002	50+	Mixed, Terceira, Azores, 936	ESSG	2.7	0.4	1.6
Braun (23)	Germany	1998	18+	Blood donors, 1871	ESSG			1.9
AFRICA								
Adebajo (4)	Sub-saharal Africa	1994	A	Negro, rural	Doctor dg			0.00
Mijiyawa (5)	Togo	2000	A	Negro, rural	Doctor dg			0.00
APLAR region (south-east Asia and Pacific)								
Davatachi (1)	Phillipines	1997	15+	Urban, Manila, 3006	Doctor dg			0.03
Akhter (6)	Pakistan	2011	15+	Rural, 2090	/			0.10
Veerapen (7)	Malasya	1992	15+	Rural, Banting, 2594	Doctor dg			0.12
Davatachi (1)	Tailand	1998	15+	Rural, 2463	/			0.12
Dai (9)	China	2003	15+	Urban, Shangai, 7603	Doctor dg			0.11
Zeng (10)	China	1995	16+	Urban, Shantou 2040				0.26
Davatachi (1)	Iran	1995	15+	Urban, 7000	/			0.34
Onen (12)	Turkey	2008	20+	Urban, Izmir, 2887	ESSG	0.88	1.22	1.05*
Onen (13)		2015		University Employees, 381	ASAS			1.35
Davatachi (1)	APLAR	2006	15+	APLAR	/			0.19*
Alexeeva (2)	Russia	1994	P	Chukotka, Russia				2.5
NORTH AMERICA								
Strand (24)	USA	2013	18+	Mixed, pt.records, 816	ASAS			0.70
Helmick (25)	USA	2005	18+	NHIS	Doctor dg			0.35-1.31
Boyer (3)	Alaska	1994	20+	Eskimos, 6749	ESSG/AMOR			2.50

A – adult; P – population;
*Prevalence estimates standardized for age and sex in terms of the country population; Doctor dg, diagnosis made by a doctor; ESSG, European Spondyloarthropathy Study Group Classification criteria; ASAS, SpondyloArthritis international Society criteria; AMOR, Spondyloarthropathy criteria by Amor et al;

Table 2. Ankylosing spondylitis prevalence

Reference	Country	Year	Age	Method	Prevalence (%)
EUROPE					
Saraux (15)	France	2001	18+	Questionnaire	0.08*
Zlatkovic-Svenda (17)	Serbia	2008	18+	Questionnaire	0.08*
Hanova (34)	Czech Republic	2003	16+	Register	0.09
Haglund (18)	Sweden	2011	15+	Register	0.12
Kaipiainen (35)	Finland	1997	30+	Sample	0.15
Trontzas (36)	Greece	2005	19+	Questionnaire	0.24*
Anagnostopoulos (37)		2010	A	Questionnaire	0.29
Alamanos (38)		2002	16+	Register	0.29*
Backland (39)	Norway	2005	20+	Register Urban	0.26
Gran (40)		1985			1.1-1.4
De Angelis (21)	Italy	2007	18+	Questionnaire	0.37
Bruges-Armas (22)	Portugal	2002	50+	Questionnaire	0.60
Braun (23)	Germany	1998	18+	Blood donors	0.86
AFRICA					
Stein (28)	Zimbabwe	1990		Population	0.00
Adebajo (29)	Nigeria	1991		Population	0.00
Mijiyawa (30)	Togo	1993		Population	0.00
APLAR region (south-east Asia and Pacific)					
Hukuda (31)	Japan	2001	A	Register	0.01
Dai (9)	Shangai	2003		Urban	0.11*
		1985	16+	Rural	0.22
		1995	16+	Urban	0.2
Yao-Jun (32)	China	2005	16+	Urban	0.2*
Chou (33)	Taiwan	1994	20+	Urban	0.40
				Suburban	0.19
				Rural	0.54
Onen (12)	Turkey	2008	20+	Urban	0.49*
Alexeeva (2)	Chukotka, Russia	1994	P	Population	1.1
NORTH AMERICA					
Boyer (3)	Alaska	1994	20+	Register	0.4
Strand (24)	USA	2013	18+	Pt records	0.35
Helmick (25)		2005	18+	NHIS	0.52*
Lawrence (41)	USA, white race	1998	A	Sample	0.13*
Gofton (27)	Canada, Haida Indians	1964	15+	Population	6.2

A – adult; P – population;
*Prevalence estimates standardized for age and sex in terms of the country population

Table 3. Psoriatic arthritis prevalence

Reference	Country	Year	Age	Method	Prevalence (%)
EUROPE					
Hellgren (45)	Sweden	1969	P		0.02
van Romunde (46)	Netherlands	1984	20+	Sample	0.05
Zlatkovic-Svenda (17)	Serbia	2008	18+	Questionnaire	0.09
Pedersen (47)	Denmark	2002	Twins	Questionnaire	0.15
Madland (48)	Norway	2002	A	Register	0.19*
Hanova (34)	Czech Republic	2003	16+	Register	0.05*
Saraux (15)	France	2001	18+	Questionnaire	0.19*
Braun (23)	Germany	1998	18+	Blood donors	0.29
Alamanos (49)	Greece	2001	A	Register	0.06*
Trontzas (37)		2005	19+	Questionnaire	0.17*
Anagnostopoulos (38)		2010	A	Questionnaire	0.35
Salaffi (50)	Italy	2005	18+	Questionnaire	0.37
De Angelis (21)		2007	18+	Questionnaire	0.42
AFRICA					
Adebajo (29)	Subsaharial Africa	1990			0.00
Lamurezo (42)	Uganda	1980			0.00
APLAR region (south-east Asia and Pacific)					
Hukuda (43)	Japan	2001	A	Register	0.001
Zheng (44)	China	2006	A	Study	0.01-0.1
NORTH AMERICA					
Lawrence (41)	USA white race	1998	A	Sample	0.07*
Gelfand (51)		2005	P	Questionnaire	0.25
Shbeeb (52)	Minesota	1991	A	Register	0.16*
Boyer (3)	Alaska	1994	20+	Register	0.1
SOUTH AMERICA					
Soriano (53)	Argentina	2006	P	Register	0.07

A – adult; P – population;

*Prevalence estimates standardized for age and sex in terms of the country population

Figure 1. Spondyloarthritis prevalence in the world given in percentages

NOTE: The specific population estimate may not represent the full population estimate for a particular country (see Table 1)

Figure 2. Ankylosing spondylitis prevalence in the world given in percentages

NOTE: The specific population estimate may not represent the full population estimate for a particular country (see Table 2)

Figure 3. Psoriatic arthritis prevalence in the world given in percentages

NOTE: The specific population estimate may not represent the full population estimate for a particular country (see Table 3)

