

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Spondyloarthritis in the Democratic Republic of Congo

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-020329
Article Type:	Research
Date Submitted by the Author:	09-Nov-2017
Complete List of Authors:	Lebughe, Pierrot; Universite de Kinshasa, Internal Medicine de Vlam, Kurt; Katholieke Universiteit Leuven, Skeletal Biology and Engineering Research Center, Department of Development and Regeneration; Universitaire Ziekenhuizen Leuven, Department of Rheumatology Westhovens, Rene; Skeletal Biology and Engineering Research Center, Department of Development and Regeneration; Universitaire Ziekenhuizen Leuven, Department of Rheumatology Mbuyi-Muamba, Jean-Marie ; University Hospital of Kinshasa, Kinshasa, DR Congo, Department of internal medicine,Rheumatology unit Malemba, Jean Jacques; University Hospital of Kinshasa, Kinshasa, DR Congo, Department of internal medicine,Rheumatology unit
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Rheumatology, Immunology (including allergy)
Keywords:	Epidemiology < TROPICAL MEDICINE, RHEUMATOLOGY, IMMUNOLOGY

SCHOLARONE™
Manuscripts

Only

Spondyloarthritis in the Democratic Republic of Congo

Authors

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1. **Pierrot Lebughe**

Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa, Kinshasa, DR Congo. lebughe7@gmail.com

2. **Kurt de Vlam**

University Hospitals Leuven, Division of Rheumatology, Herestraat 49 box 7003, 3000 Leuven, Belgium. kurt.devlam@uzleuven.be

3. **René Westhovens**

KU Leuven, Department of Development and Regeneration, Skeletal Biology and Engineering Research Center, University Hospitals Leuven, Division of Rheumatology Herestraat 49 box 7003, 3000 Leuven, Belgium. rene.westhovens@uzleuven.be.

4. **Jean-Marie Mbuyi-Muamba**

Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa, Kinshasa, DR Congo

E-mail: mbuyi_muamba@yahoo.fr

5. **Jean-Jacques Malemba**

Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa, Kinshasa, DR Congo

E-mail: jeje_malemba2003@hotmail.com

Corresponding author:

Pierrot Lebughe

Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa, Po Box 123, Kinshasa XI, DR Congo

lebughe7@gmail.com

Phone: +243 81 025 11 91

Word count (for both abstract and the main text): words

Abstract

Objectives: To determine the spectrum of SpA in outpatients with rheumatic complaints attending two rheumatology practices.

Design: Descriptive cross-sectional multicenter outpatient study.

Setting: The present study analyzed 6 months of cross-sectional data (December 1st, 2012 till May 31th, 2013).

Participants: 984 consecutive patients were recorded from the two rheumatology practices of Kinshasa, Democratic republic of Congo. Sacroiliac joint radiographic lesions were scored with the modified New York criteria. BASDAI and BASFI were evaluated in axial SpA.

Interventions No interventions

1
2
3 **Primary and secondary outcome measures:** The primary efficacy end point was the prevalence of
4 SpA and the secondary efficacy were the spectrum of SpA and its subtypes.

5
6 **Results** One hundred five patients (10.7%) were diagnosed among 984 rheumatologic outpatients
7 with a sex ratio (male to female) of 1.4. The average age at the onset of the disease was 41.3±12.4
8 years. Non-radiographical axial spondyloarthritis was the most frequent subtype (4.98%) followed by
9 reactive arthritis (4.27%). Other subtypes were: ankylosing spondylitis (1.02%), psoriatic arthritis
10 (0.1%), SAPHO syndrome (0.1%) and IBD associated arthritis (0.1%). Mean BASDAI and BASFI in axial
11 SpA were 42.7/100 and 46.4/100 respectively. Peripheral enthesitis was found in 43% of SpA patients
12 and uveitis (10.4%) was the most frequent extra-articular manifestation. We did not detect any
13 family history. Median erythrocyte sedimentation rate and C reactive protein were 37 (range: 7-110)
14 mm/h and 22 (range: 4-48) mg/l respectively.

15
16 **Conclusions** This hospital-based study suggests a substantial occurrence of some subtypes of SpA in
17 central Africa. A population-based study is needed.

18
19 **Keywords:** Spondyloarthritis. Democratic Republic of Congo.

20 21 22 23 24 25 26 27 **Strengths and limitations of this study**

- 28
29 • To the best of our knowledge, this is the first study describing more detailed the spectrum of
30 Spondyloarthritis in Kinshasa, Democratic republic of Congo.
- 31
32 • In this hospital-based study, diagnostic criteria applied by rheumatologist have improved
33 clinical diagnosis while the application of the criteria of Amor and ESSG in medical records
34 might lead to underdiagnosis.
- 35
36 • A population-based study will be need to describe the phenotype and genotype of
37 Spondyloarthritis in central Africa.

38 39 40 41 42 43 **Introduction**

44
45 SpA is a heterogeneous group of mostly chronic interrelated inflammatory rheumatic diseases that
46 share a common genetic predisposition and specific clinical characteristics such as spinal
47 inflammation, asymmetric peripheral arthritis, dactylitis and enthesitis (1) but also common extra-
48 articular features as uveitis, psoriasis and inflammatory bowel disease.

49
50 Based on the "Assessment of SpondyloArthritis international Society" (ASAS) classification criteria,
51 SpA can be divided into two subsets: axial SpA (axSpA) including ankylosing spondylitis (AS) and non-
52 radiographical axial spondyloarthritis (nr-axSpA) and also peripheral SpA, including reactive arthritis
53 (ReA), psoriatic arthritis (PsA), enteropathic arthritis and juvenile SpA (2).

1
2
3 The spectrum of SpA in sub-Saharan Africa remains poorly defined. In African black populations, SpA
4 is considered to be extremely rare explained in part by the low prevalence of HLA-B27 (3-6). A
5 completely different environment on top of a different genetic background might also be responsible
6 for the rarity as well for a different disease presentation (7-11). Few studies reported on the
7 epidemiological, clinical, radiological features of SpA in sub-Saharan populations (3-6, 12). These
8 studies are mostly older, biased because based on hospital cohorts and suggest differential
9 epidemiological and clinical aspects of SpA in our region. In DR Congo, data on SpA are also scarce. A
10 first hospital-based study reported a prevalence of 7.5% among patients attending the University
11 Hospital of Kinshasa (UHK) for rheumatic complaints (13). The purpose of this present study was to
12 report in a more detailed way the spectrum of SpA and its subtypes in patients attending two
13 rheumatology units in DR Congo.
14
15
16
17
18
19
20
21

22 **Methods**

23
24 This was a cross-sectional study conducted in the department of internal medicine of the University
25 Hospital of Kinshasa and the Provincial General Hospital Kinshasa (PGHK) (Kinshasa, RD Congo, Africa)
26 during six months, from December 1st, 2012 till May 31th, 2013.
27
28
29

30 These two hospitals were chosen because of the existence of a Rheumatology unit. In the DR Congo
31 there are no other rheumatology units and in total 5 rheumatologists are working in Kinshasa.
32 Problems in the organization of care as well as the lack of a health insurance system do not allow
33 patients with rheumatic complaints good accessibility to health care.
34
35

36 All the patients visiting the outpatients clinics of these hospitals for rheumatic complaints during the
37 study period were included. A complete clinical examination by the rheumatologist was performed.
38 Details of joint symptoms, back pain and stiffness, personal and family histories of arthritis, skin
39 lesions, symptoms of acute anterior uveitis, enthesitis, dactylitis, Crohn's disease/colitis, diarrhea,
40 urethritis, good response to non-steroidal anti-inflammatory drugs (NSAIDs) and a positive family
41 history of SpA were recorded. The diagnosis of SpA was according to Amor and ESSG. When the
42 criteria were not fulfilled, the rheumatologist could still make the diagnosis according to his clinical
43 experience. According to the 2009 criteria of the ASAS, ax-SpA is categorized into nr-axSpA and AS, in
44 which the major distinguishing feature is the presence or absence of radiographic sacroiliitis (14, 15).
45 PsA diagnosis was according to the CASPAR classification (16). All patients with buttock pain and/or
46 low back pain underwent image evaluation of the pelvis in anterior-posterior view by conventional X-
47 rays. Sacroiliac joint radiographic lesions were scored with modified New York criteria. Others joints
48 X-rays were performed when additional manifestations were presents (peripheral arthritis,
49 enthesitis, and dactylitis). Patients with axSpA were also asked to complete the BASDAI and BASFI
50
51
52
53
54
55
56
57
58
59
60

1
2
3 (17). All patients were assisted by rheumatologist to complete the two questionnaires. For the
4 patients who had a difficulty to understand the French language, the rheumatologist had proceeded
5 to a translation in Lingala to explain different questions contained. Blood tests including erythrocyte
6 sedimentation rate (ESR) and the serum CRP were also performed in all patients. HLA-B27 typing was
7 not realized.
8
9

10 Qualitative data are described as n (%) and quantitative data as mean (SD) or median
11 (quartile1_quartile3) as appropriate. Chi-square test was used to compare the comparison of the
12 proportions. A student-t test was used to compare the averages. The p-value was fixed to 0.05. The
13 study was conducted in accordance with the National Ethics Committee (ESP/CE/030/13).
14
15
16
17

18 **Results**

19
20 During the study period, 984 patients visited one of the Rheumatology units for rheumatic
21 complaints. The diagnosis of SpA was made in 105 patients (10.7%). The frequencies for the
22 retrospective subtypes were 4.98% for nr-axSpA, 4.27% for ReA, 1.02% for AS. One patient was seen
23 with PsA, SAPHO syndrome or IBD associated arthritis. Sixty two patients (59%) were male with a
24 male/female sex ratio of 1.4. The mean age of the patients was 44.7±13.5 years; their median
25 disease duration was 3.6 years (range: 0.3 - 15 years). Their average age at the onset of symptom
26 was 41.3±12.4 years. Table 1 reports the different types of SpA encountered. Inflammatory back
27 pain (86.2%) and buttock pain (72.4%) were the most frequent symptoms seen in axSpA while
28 asymmetrical oligoarthritis (80.8%) and plantar talalgias (66.0%) as the most frequently encountered
29 features in peripheral SpA. Table 2 shows the demographic, clinical data and clinical assessment
30 scores of patients with axSpA. Fifty nine patients (56.2%) presented with axSpA and all of them had
31 standard radiographs of sacroiliac joints. Ten patients (6 males and 4 females) showed radiographic
32 sacroiliitis as defined by modified New York criteria and thus classified as AS while 49 patients (27
33 males) with axSpA (83.1%) had an absence of radiographic sacroiliitis so defining nr-axSpA. Table 2
34 report demographic and clinical characteristics of patients with axSpA. Patients with AS complained
35 of chronic low back pain (CLBP) for 8.4±3.2 years compared with 4.7±3.3 years for patients with nr-
36 axSpA (p<0.01). All patients with axSpA had inflammatory back pain according to ASAS criteria. One
37 patient presented a dorsolumbar pain. The mean distance C7-wall was 4.5±1.6 cm with extremes of 3
38 and 8 cm. The mean distance between the nape and the wall was 19±7.7 cm with extremes of 12 and
39 30 with a mean Schobër index of 10+4.2cm (SD 3.2cm). Six patients had radiographic sacroiliitis at
40 stage 2 bilateral and 4 patients had radiographic sacroiliitis at stage 3 according to the modified
41 criteria of New York. Other radiographic findings were in particular signs of iliac and ischio-pubic
42 enthesitis in 5 cases. Syndesmophytes were present among 5 patients while no hip joint involvement
43 was found in the standard radiographs. Elevated CRP and ESR values were found in 75.5% and 36.7%
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

of patients with nr-axSpA respectively 80.0% and 40.0% of patients with AS had an elevated CRP and ESR, respectively. In the 42 ReA patients (26 males and 17 females), 21 had urogenital manifestations, 14 had enteropathic manifestations and 4 patients had a classical Reiter's syndrome with articular, ocular and urogenital manifestations. Any idea about the bacteria was found in this study. The only case of PsA was found in a 32 year-old patient developing psoriasis 3 years earlier than the onset of articular features with asymmetrical oligoarthritis in the upper limb and typically in the distal interphalangeal joints. Altogether, extra-articular manifestations encountered were uveitis (12.4%), enterocolopathy (0.95%), pustulosis (0.95%) and psoriatic lesions (0.95%). No family history of SpA was found.

Table 1. Different subtypes of SpA in UHK and PGHK in Kinshasa

Subtypes of SpA	N (Rf)	Sex distribution				Mean age (years)±SD
		M	F	Ratio	P	
Nr-axSpA	49 (46.7)	27	22	1:0.8	0.23	40.5±7.5
ReA	42 (40.0)	20	22	1:1.1	0.47	40.2±13.1
AS	10 (9.5)	6	4	1:0.7	0.45	46.2±4.7
PsA	1 (0.95)	0	1			32
SAPHO Syndrome	1 (0.95)	1	0			35
Enteropathic arthritis	1 (0.95)	0	1			25
Juvenile SpA	1 (0.95)	1	0			13

N Total number of patients with SpA, M men, W women, Rf relative frequency to total number of patients with SpA, nr-axSpA non-radiographical axial spondyloarthritis, ReA reactive arthritis, AS ankylosing spondylitis, PsA psoriatic arthritis, SAPHO syndrome synovitis acne pustulosis hyperostosis osteitis syndrome.

Table 2. Demographic and clinical features of patients with axial Spondyloarthritis.

	axSpA (total group, n=59)	nr-axSpA (n= 49)	AS (n= 10)	P
Age, mean \pm SD years	45.6 \pm 6.1	41.5 \pm 7.5	48.2 \pm 4.7	0.03
Age of onset \pm SD years	38 \pm 4.5	37.2 \pm 5.6	40.1 \pm 6.3	0.27
Male sex	33 (55.9)	27 (55.1)	6 (60.0)	0.45
Symptom duration > 5years	38 (64.4)	18 (36.7)	9 (90.0)	0.02
Clinical features				
Peripheral arthritis	18 (30.5)	16 (32.7)	2 (20.0)	0.23
Enthesitis	13 (22.4)	10 (20.4)	3 (30.0)	0.43
Uveitis	9 (15.5)	6 (12.2)	3 (30.0)	0.22
Psoriasis	1 (1.7)	1 (1.9)	0 (0.0)	
IBD	1 (1.7)	1 (1.9)	0 (0.0)	
BASDAI	42.7 \pm 9.2	39 \pm 11.4	44 \pm 15.5	0.42
BASFI	46.4 \pm 12.9	44.5 \pm 13.8	48.2 \pm 10.2	0.53
ESR (mm/h) median, range	37 (7-110)	36 (7-68)	41 (13-110)	0.40
CRP (mg/L) median, range	22(4-48)	20 (6-48)	26 (6-48)	0.26
<i>axSpA</i> , axial spondyloarthritis, <i>nr-axSpA</i> non-radiographical axial spondyloarthritis, <i>AS</i> ankylosing spondylitis, <i>IBD</i> inflammatory bowel disease.				

Discussion

The prevalence of SpA was 10.7% among rheumatic patients during the 6-month period of the current study and is higher than that found by Malemba and al. (7.5%) based on an extensive review of patients medical records seen by rheumatologists at the UHK. In this hospital-based study, diagnostic criteria applied by rheumatologist were used to improve clinical diagnosis while the application of the criteria of Amor and ESSG in medical records might lead to underdiagnosis. Moreover, in our environment HLA typing is not feasible and because of the low frequency of HLA B27 also not very well performing. Because of all this, ESSG and Amor criteria would need specific validation studies in our region. We observed 105 cases of SpA and a male/female sex ratio of 1.4. More men were affected in the total as confirmed in most of the literature reported from Africa and western countries (18-22). The mean age and the age at the onset of symptom were higher than in the series reported in the western countries, but in agreement with the literature reported from the

1
2
3 sub-Saharan region (4, 18-22). A completely different environment (differences in sanitary
4 equipments, differences in infections occurring in this populations) on top of a different genetic
5 background might be responsible for a different disease presentation and perhaps as a consequence
6 also later diagnosis (7). One might overlook specific clinical presentations and as already mentioned
7 classical classification criteria are not validated in this region. It is also necessary to underline the
8 relatively long delay between the onset of symptom and the consultation as found by several African
9 authors, explained mainly by the poverty of population and problems regarding health care in this
10 part of the world (21). The high frequency of endemic infectious diseases in tropical areas and the
11 precariousness of community and individual measures of hygiene would explain the high frequency
12 of ReA. Despite occurring frequently, ReA in our region is expected to present with milder clinical
13 features probably because of a protective role played by the local genetic factors (7, 8). Further
14 genetic research could be interesting in this field. In this study we observed 10 cases of AS (1.02%).
15 This scarcity seems to be related to the low frequency of HLA B27 gene in this population (23). Less
16 male predominance has been observed among Congolese patients with SpA, AS and nr-axSpA
17 compared to Caucasians (3). However different demographical and methodological characteristics
18 could also contribute to the explanations of gender differences observed. The proportion of females
19 could be underestimated because most of patients with pelvic inflammatory disease would be seen
20 in Gynecology departments in our country where full rheumatologic evaluations and sacroiliac
21 radiographs are not systematically performed. Patients with AS had a mean age of 48.2 years (SD 4.7)
22 with the age of onset typically older as reported in other sub Saharan literature and with no family
23 history of SpA and also a relative rarity of extra-articular features, notably uveitis also in accordance
24 with data of the literature of SpA in sub-Saharan Africa (4,6,20-22).

25
26
27
28
29
30
31
32
33
34
35
36
37
38 Pertinent differences between AS and nr-axSpA (83.1% of axSpA) in this study included significantly
39 longer disease duration and mean age at consultation for AS ($p < 0.05$). Apart from the fact of AS
40 developing after an initial period of disease with negative radiographical findings, this longer disease
41 duration before consultation can also be explained by the many problems concerning organization of
42 health care, the poverty of the Congolese population having no access to treatment, as well as by
43 cultural specificities with difficulties in understanding the concept of chronicity of a disease (24). No
44 significant difference was observed regarding extra articular features, parameters of disease activity
45 and function as well as inflammatory markers including BASDAI, BASFI, ESR and CRP between these
46 two groups. This is of course difficult to judge in a cross-sectional study of different disease entities
47 when AS might be just the "natural evolution" of nr-axSpA (25-27). Only one case of PsA was
48 reported in this study in a woman of 32 years old with HIV negativity. The skin lesions antedated the
49 joint symptoms for three years, including peripheral joint involvement and sacroiliitis. This scarcity of
50 psoriasis and PsA is in accordance to sub Saharan literature reports (3, 4, 20-22). Further studies
51
52
53
54
55
56
57
58
59
60

1
2
3 must be performed both in Rheumatology and Dermatology to identify case ascertainment of PsA in
4 this spectrum in Congolese population.
5

6 **Conclusion**

7 SpA is not rare in outpatients attending Rheumatology units in DR Congo. A population-based study
8 would improve the understanding of this disease spectrum in central Africa. Such a study will need to
9 take in to account the differential infectious background, problems related to the health care system
10 and poverty of the population and differential genetics in this environment. Classification criteria
11 validated in the western world will not necessarily perform the same in our region.
12
13
14
15

16 **Author affiliations**

17
18 1 Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa,
19 Kinshasa, DR Congo
20

21
22 2 University Hospitals Leuven, Division of Rheumatology, 3000 Leuven, Belgium
23

24 3 KU Leuven, Department of Development and Regeneration, Skeletal Biology and Engineering
25 Research Center, University Hospitals Leuven, Division of Rheumatology, 3000 Leuven, Belgium
26
27

28 **Acknowledgements**

29
30 The authors would like to thank Dr Thierry Lusiense, Department of internal medicine, for helping
31 with acquisition of data from the Rheumatology unit at Provincial General Hospital Kinshasa.
32

33 **Contributors**

34 PL wrote protocol, recruited and enrolled participants, collected data, and drafted the report. JJM
35 analysed and interpreted the data. JMM served as medical, participated in the design and helped to
36 draft the manuscript. KDV and RW edited the final version of the manuscript. PL had full
37 responsibility for the integrity of the data and the accuracy of the data analysis.
38
39
40
41
42

43
44 **Funding** .This research had received no specific grant from any funding agency in the public,
45 commercial or not-for-profit sectors
46

47 **Competing interests.** None declared.
48

49 **Patient consent.** Obtained.
50

51 **Ethics approval.** National Ethic Committee (ESP/CE/030/13).
52

53 **Data sharing statement.** No additional data are available
54

55 **References**

56
57
58
59
60

1. Sieper J, Rudwaleit M, Khan MA, Braun J (2006) Concepts and epidemiology of spondyloarthritis. *Best Pract Res Clin Rheumatol* 20:401–17
2. Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, et al (2009) The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 68:777–83
3. Stolwijk C, van Onna M, Boonen A, van Tubergen A (2015) Global Prevalence of Spondyloarthritis: A Systematic Review and Meta-Regression Analysis. *Arthritis Care Res (Hoboken)* Dec 29
4. Tikly M, Njobvu P, McGill P (2014) Spondyloarthritis in Sub-Saharan Africa. *Curr Rheumatol Rep* 16:421
5. Rachid B, El Zorkany B, Youseif E, Tikly M (2012) Early diagnosis and treatment of ankylosing spondylitis in Africa and the Middle East. *Clin Rheumatol* 31:1633–9
6. Mijiyawa M, Oniankitan O, Khan MA (2000) Spondyloarthropathies in sub-Saharan Africa. *Curr Opin Rheumatol* 12:281–6
7. Cao K, Moormann AM, Lyke KE, et al (2004) Differentiation between African populations is evidenced by the diversity of alleles and haplotypes of HLA class I loci. *Tissue Antigens* 63:293–325
8. Mathieu A, Paladini F, Vacca A, Cauli A, Fiorillo MT, Sorrentino R (2009) The interplay between the geographic distribution of HLA-B27 alleles and their role in infectious and autoimmune diseases: A unifying hypothesis. *Autoimmun Rev* 8:420-5
9. Brown MA, Jepson A, Young A, Whittle HC, Greenwood BM, Wordsworth BP (1997) Ankylosing spondylitis in West Africans—evidence for a non-HLA-B27 protective effect. *Ann Rheum Dis* 56(1):68–70.
10. Solomon L, Beighton P, Valkenburg HA, Robin G, Soskolne CL (1975) Rheumatic disorders in the South African Negro. Part I. Rheumatoid arthritis and ankylosing spondylitis. *S Afr Med J* 49(32):1292–6
11. Díaz-Peña R, Blanco-Gelaz MA, Njobvu P, López-Vazquez A, Suárez-Alvarez B, López-Larrea C (2008) Influence of HLA-B*5703 and HLA-B*1403 on Susceptibility to Spondyloarthropathies in the Zambian Population. *J Rheumatol* 35(11):2236-40
12. Singwe-Ngandeu M, Meli J, Ntsiba H, Nouedoui C, Yollo AV, Sida MB, et al (2007) Rheumatic diseases in patients attending a clinic at a referral hospital in Yaoundé, Cameroon. *East Afr Med J* 84 (9):404–9
13. Malemba JJ, Mbuyi-Muamba JM (2008) Clinical and epidemiological features of rheumatic diseases in patients attending the university hospital in Kinshasa. *Clin Rheumatol* 27:47–54

- 1
2
3 14. Rudwaleit M, Landewé R, van der Heijde D, Listing J, Brandt J, Braun J, et al (2009) The
4 development of Assessment of SpondyloArthritis international Society classification criteria
5 for axial spondyloarthritis (part I): classification of paper patients by expert opinion including
6 uncertainty appraisal. *Ann Rheum Dis* 68: 770–6
7
- 8
9 15. Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, et al (2009) The
10 development of Assessment of SpondyloArthritis international Society classification criteria
11 for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 68: 777–83
12
- 13 16. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H (2006) Classification
14 criteria for psoriatic arthritis: development of new criteria from a large international study.
15 *Arthr & Rheum* 54: 2665-73
16
- 17 17. Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P, Jenkinson T (1994) A new
18 approach to defining functional ability in ankylosing spondylitis: the development of the Bath
19 Ankylosing Spondylitis Functional Index. *J Rheumatol* 21(12):2281-5
20
- 21 18. Dean LE, Jones GT, MacDonald AG, Downham C, Sturrock RD, Macfarlane GJ (2014) Global
22 prevalence of ankylosing spondylitis. *Rheumatology* 53:650-7
23
- 24 19. Usenbo A, Kramer V, Young T, Musekiwa A (2015) Prevalence of Arthritis in Africa: A
25 Systematic Review and Meta-Analysis. *PLoS One* 10(8):e0133858
26
- 27 20. Mijiyawa M, Oniankitan O, Khan MA (2000) Spondyloarthropathies in sub-Saharan Africa.
28 *Curr Opin Rheumatol* 12(4):281-6
29
- 30 21. Belachew DA, Sandu N, Schaller B, Guta Z (2009) Ankylosing spondylitis in sub-Saharan Africa.
31 *Postgrad Med J* 85(1005):353-7
32
- 33 22. Ouédraogo DD, Meyer O (2012) Psoriatic arthritis in Sub-Saharan Africa. *Joint Bone Spine*
34 79(1):17-9
35
- 36 23. Mbayo K, Mbuyi-Muamba JM, Lurhuma AZ, Halle L, Kaplan C, Dequeker J (1998) Low
37 frequency of HLA-B27 and scarcity of ankylosing spondylitis in a Zairean Bantu population.
38 *Clin Rheumatol* 17(4):309-10
39
- 40 24. Lebughe LP, Malemba JJ, Divengi JP, Mbuyi-Muamba JM (2016) Itineraries of the rheumatic
41 patients towards the rheumatologist in DR Congo. *Afr J Rheumatol* 4(2): 63-65
42
- 43 25. Kiltz U, Baraliakos X, Karakostas P, Igelmann M, Kalthoff L, Klink C et al (2012) Do patients
44 with non-radiographic axial spondylarthritis differ from patients with ankylosing spondylitis?
45 *Arthritis Care Res* 64(9):1415-22
46
- 47 26. Malaviya AN, Kalyani A, Rawat R, Gogia SB (2015) Comparison of patients with ankylosing
48 spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) from a single
49 rheumatology clinic in New Delhi. *Int J Rheum Dis* 18(7):736-41
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

27. Burgos-Varga R, Wei JC, Rahman MU, Akkoc N, Haq SA, Hammoudeh M et al (2016) The prevalence and clinical characteristics of non-radiographic axial spondyloarthritis among patients with inflammatory back pain in rheumatology practices: a multinational, multicenter 18(1):132

For peer review only

BMJ Open

Spondyloarthritis in the Democratic Republic of Congo: a prospective hospital-based study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-020329.R1
Article Type:	Research
Date Submitted by the Author:	17-Jan-2018
Complete List of Authors:	Lebughe, Pierrot; University Hospital of Kinshasa, Department of internal medicine,Rheumatology unit de Vlam, Kurt; University Hospitals Leuven, Division of Rheumatology, KU Leuven, Department of Development and Regeneration, Skeletal Biology and Engineering Research Center Herestraat 49, box 7003 Westhovens, Rene; KU Leuven, Department of Development and Regeneration, Skeletal Biology and Engineering Research Center; University Hospitals Leuven, Division of Rheumatology Herestraat 49, box 7003, Mbuyi-Muamba, Jean-Marie ; University Hospital of Kinshasa, Kinshasa, DR Congo, Department of internal medicine,Rheumatology unit Malemba, Jean Jacques; University Hospital of Kinshasa, Kinshasa, DR Congo, Department of internal medicine,Rheumatology unit
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Rheumatology, Immunology (including allergy)
Keywords:	Epidemiology < TROPICAL MEDICINE, RHEUMATOLOGY, IMMUNOLOGY

SCHOLARONE™
Manuscripts



Spondyloarthritis in the Democratic Republic of Congo: a prospective hospital-based study

Authors

1
2
3
4
5
6
7
8
9
10
11

1. Pierrot Lebughe

Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa, Kinshasa, DR Congo. lebughe7@gmail.com

12
13
14

2. Kurt de Vlam

University Hospitals Leuven, Division of Rheumatology, KU Leuven, Department of Development and Regeneration, Skeletal Biology and Engineering Research Center Herestraat 49, box 7003, 3000 Leuven, Belgium. kurt.devlam@uzleuven.be

15
16
17
18

3. René Westhovens

KU Leuven, Department of Development and Regeneration, Skeletal Biology and Engineering Research Center, University Hospitals Leuven, Division of Rheumatology Herestraat 49, box 7003, 3000 Leuven, Belgium. rene.westhovens@uzleuven.be

19
20
21
22

4. Jean-Marie Mbuyi-Muamba

Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa, Kinshasa, DR Congo
E-mail: mbuyi_muamba@yahoo.fr

23
24
25
26

5. Jean-Jacques Malemba

Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa, Kinshasa, DR Congo
E-mail: jeje_malemba2003@hotmail.com

27
28
29
30
31
32

Corresponding author:

33
34

Pierrot Lebughe

Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa, PO Box 123, Kinshasa XI, DR Congo
lebughe7@gmail.com
Phone: +243 81 025 11 91

35
36
37
38
39
40

Word count (for both abstract and the main text):

41
42
43

Abstract

44
45
46
47

Objectives: To determine the spectrum of SpA in outpatients with rheumatic complaints attending two rheumatology practices in the Democratic Republic of Congo.

48
49

Design: A descriptive prospective multicenter outpatient study.

50
51

Setting: The present study analyzed 6 months data (from December 1st, 2012 till May 31st, 2013).

52
53

Participants: 984 consecutive outpatients were studied.

54
55
56
57
58
59
60

Interventions: none

1
2
3 **Primary and secondary outcome measures:** A clinical diagnosis of SpA was made and several
4 classification criteria were applied afterwards. Sacroiliac joint radiographic lesions were scored with
5 the modified New York criteria. BASDAI and BASFI were evaluated in axial SpA. The primary end point
6 was the prevalence of SpA and the secondary endpoints were the spectrum of SpA and its subtypes.
7

8 **Results:** One hundred and five patients (10.7%) were diagnosed among 984 consecutive outpatients
9 with a sex ratio (male to female) of 1.4. The average age at disease onset was 41.3±12.4 years. Non-
10 radiographical axial spondyloarthritis was the most frequent subtype (5.0%) followed by reactive
11 arthritis (4.3%). Other subtypes were: ankylosing spondylitis (1.0%), psoriatic arthritis (0.1%), SAPHO
12 syndrome (0.1%) and IBD associated arthritis (0.1%). Mean BASDAI and BASFI in axial SpA were
13 42.7/100 and 46.4/100 respectively. Peripheral enthesitis was found in 43% of SpA patients and
14 uveitis (10.4%) was the most frequent extra-articular manifestation. We did not detect any family
15 history. Median erythrocyte sedimentation rate and C reactive protein were 37(range: 7-110) mm/h
16 and 22 (range: 4-48) mg/l respectively.
17

18 **Conclusions:** This hospital-based study suggests a substantial occurrence of some subtypes of SpA in
19 central Africa. A population-based study is needed.
20

21 **Keywords:** Spondyloarthritis. Democratic Republic of Congo.
22

23 **Strengths and limitations of this study**

- 24
- 25 • To the best of our knowledge, this is the first more detailed study describing the spectrum of
26 Spondyloarthritis in the Democratic Republic of Congo.
 - 27 • In this hospital-based study, clinical diagnosis was followed by diagnostic criteria applied by
28 rheumatologists strengthening the results, while the application of classification in medical
29 records might have led to misdiagnosis.
 - 30 • HLA typing and MRI were not performed due to lack of availability and economic constraints.
31 On the other hand applying classical ASAS criteria to an African population would perhaps
32 not be accurate and specific validation is needed in our population.
 - 33 • Relationships with sexually transmitted and other infections are lacking in our study and
34 future work needs to draw attention to this important issue.
 - 35 • A population-based study will be needed to accurately evaluate the phenotype and genotype
36 of Spondyloarthritis in central Africa.
- 37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

SpA is a heterogeneous group of mostly chronic interrelated inflammatory rheumatic diseases that share a common genetic predisposition and specific clinical characteristics such as spinal inflammation, asymmetric peripheral arthritis, dactylitis and enthesitis (1) but also common extra-articular features as uveitis, psoriasis and inflammatory bowel disease.

Based on the "Assessment of SpondyloArthritis International Society" (ASAS) classification criteria, SpA can be divided into two subsets: axial SpA (axSpA) including ankylosing spondylitis (AS) and non-radiographical axial spondyloarthritis (nr-axSpA) and also peripheral SpA (pSpA), including reactive arthritis (ReA), psoriatic arthritis (PsA), enteropathic arthritis and juvenile SpA (2).

The spectrum of SpA in sub-Saharan Africa remains poorly defined. In African black populations, SpA is considered to be extremely rare explained in part by the low prevalence of HLA-B27 (3-6). A completely different environment on top of a different genetic background might also be responsible for the rarity as well for a different disease presentation (7-11). Few studies reported on the epidemiological, clinical, radiological features of SpA in sub-Saharan populations (3-6, 12). These studies are mostly older, biased because based on hospital cohorts and suggest differential epidemiological and clinical aspects of SpA in our region. In DR Congo, data on SpA are also scarce. A first hospital-based study reported a prevalence of 7.5% among patients attending the University Hospital of Kinshasa (UHK) for rheumatic complaints (13). The purpose of this present study was to report in a more detailed way the spectrum of SpA and its subtypes in patients attending two rheumatology units in DR Congo.

Methods

This was a prospective study conducted in the department of internal medicine of the UHK and the Provincial General Hospital of Kinshasa (PGHK) (Kinshasa, DR Congo, Africa) for six months, from December 1st, 2012 till May 31st, 2013.

These two hospitals were chosen because of the existence of a Rheumatology unit. In the DR Congo there are no other rheumatology units and in total 5 rheumatologists are working in Kinshasa. Problems in the organization of care as well as the lack of a health insurance system do not allow patients with rheumatic complaints good accessibility to health care.

All the patients visiting the outpatients' clinics of these hospitals for rheumatic complaints during the study period were recruited consecutively. A complete clinical examination by the rheumatologist was performed. Details of joint symptoms, back pain and stiffness, personal and family histories of arthritis, skin lesions, symptoms of acute anterior uveitis, enthesitis, dactylitis, Crohn's disease/colitis, diarrhea, urethritis, good response to non-steroidal anti-inflammatory drugs (NSAIDs)

1
2
3 and a positive family history of SpA were recorded. The diagnosis of SpA was according to Amor and
4 ESSG. When the criteria were not fulfilled, the rheumatologist could still make the diagnosis
5 according to his clinical experience. AxSpA and pSpA were diagnosed when predominant
6 involvement was respectively in the axial skeleton and the peripheral joints, consisting of peripheral
7 arthritis, enthesitis and dactylitis. AxSpA was categorized into AS and nr-axSpA according to the
8 presence/absence of radiographic sacroiliitis (14, 15). The diagnosis of AS has been based upon the
9 modified New York criteria. PsA diagnosis was according to the CASPAR classification (16). All
10 patients with buttock pain and/or low back pain underwent image evaluation of the pelvis in
11 anterior-posterior view by conventional X-rays. Others joint X-rays were performed when additional
12 manifestations were present (peripheral arthritis, enthesitis, and dactylitis). Patients with axSpA
13 were also asked to complete the BASDAI and BASFI (17). All patients were assisted by
14 rheumatologists to complete the two questionnaires. For the patients who had difficulty to
15 understand the French language, the rheumatologist proceeded to a translation in Lingala to explain
16 different questions contained. Blood tests including erythrocyte sedimentation rate (ESR) and the
17 serum CRP were also performed in all patients. HLA-B27 typing was not realized.

18 Qualitative data are described as n (%) and quantitative data as mean (SD) or median
19 (quartile1_quartile3) as appropriate. Chi-square test was used to compare the comparison of the
20 proportions. A student-t test was used to compare the averages. The p-value was fixed to 0.05. The
21 study was conducted in accordance with the National Ethics Committee (ESP/CE/030/13).

32 33 34 **Results**

35 During the study period, 984 patients visited one of the Rheumatology units for rheumatic
36 complaints. The diagnosis of SpA was made in 105 patients (10.7%). 78 Patients fulfilled the Amor or
37 ESSG criteria and 27 patients were diagnosed according to clinical grounds only based on the
38 rheumatologist experience. The frequencies for the retrospective subtypes were 5.0% for nr-axSpA,
39 4.3% for ReA, 1.0% for AS. One patient was seen with PsA, SAPHO syndrome or IBD associated
40 arthritis. Sixty-two patients (59%) were male with a male/female sex ratio of 1.4. The mean age of
41 the patients was 44.7±13.5 years; their median disease duration was 3.6 years (range: 0.3 - 15 years).
42 Their average age at the onset of symptom was 41.3±12.4 years. Table 1 reports the different types
43 of SpA encountered. Inflammatory back pain (86.2%) and buttock pain (72.4%) were the most
44 frequent symptoms seen in axSpA while asymmetrical oligoarthritis (80.8%) and plantar talalgias
45 (66.0%) as the most frequently encountered features in pSpA. Table 2 shows the demographic,
46 clinical data and clinical assessment scores of patients with axSpA. Fifty-nine patients (56.2%)
47 presented with axSpA and all of them had standard radiographs of sacroiliac joints. Ten patients (6
48 males and 4 females) showed radiographic sacroiliitis as defined by modified New York criteria and
49
50
51
52
53
54
55
56
57
58
59
60

thus classified as AS while 49 patients (27 males) with axSpA (83.1%) had an absence of radiographic sacroiliitis so defining nr-axSpA. Table 2 report demographic and clinical characteristics of patients with axSpA. Patients with AS complained of chronic low back pain (CLBP) for 8.4 ± 3.2 years compared with 4.7 ± 3.3 years for patients with nr-axSpA ($p<0.01$). All patients with axSpA had inflammatory back pain according to ASAS criteria. One patient presented a dorsolumbar pain. The mean distance C7-wall was 4.5 ± 1.6 cm with extremes of 3 and 8 cm. The mean distance between the nape and the wall was 19 ± 7.7 cm with extremes of 12 and 30 with a mean Schöber index of 10 ± 4.2 cm (SD 3.2cm). Six patients had radiographic sacroiliitis at stage 2 bilateral and 4 patients had radiographic sacroiliitis at stage 3 according to the modified criteria of New York. Other radiographic findings were in particular signs of iliac and ischio-pubic enthesitis in 5 cases. Syndesmophytes were present among 5 patients while no hip joint involvement was found in the standard radiographs. Elevated CRP and ESR values were found in 75.5% and 36.7% of patients with nr-axSpA respectively 80.0% and 40.0% of patients with AS had an elevated CRP and ESR, respectively. In the 42 ReA patients (20 males and 22 females), 21 had urogenital manifestations, 17 had enteropathic manifestations and 4 patients had a classical Reiter's syndrome with articular, ocular and urogenital manifestations. Any idea about the bacteria was found in this study. The only case of PsA was found in a 32 year-old patient developing psoriasis 3 years earlier than the onset of articular features with asymmetrical oligoarthritis in the upper limb and typically in the distal interphalangeal joints. Altogether, extra-articular manifestations encountered were uveitis (12.4%), enterocolopathy (1.0%), pustulosis (1.0%), and psoriatic lesions (1.0%). No family history of SpA was found.

Table 1. Different subtypes of SpA in UHK and PGHK in Kinshasa

Subtypes of SpA	N (Rf)	Sex distribution			P	Mean age (years) \pm SD
		M	F	Ratio		
Nr-axSpA	49 (46.7)	27	22	1:0.8	0.23	40.5 \pm 7.5
ReA	42 (40.0)	20	22	1:1.1	0.47	40.2 \pm 13.1
AS	10 (9.5)	6	4	1:0.7	0.45	46.2 \pm 4.7
PsA	1 (1.0)	0	1			32
SAPHO Syndrome	1 (1.0)	1	0			35
Enteropathic arthritis	1 (1.0)	0	1			25
Juvenile SpA	1 (1.0)	1	0			13

1
2
3 *N* Total number of patients with SpA, *M* men, *W* women, *Rf* relative frequency to total number of patients with SpA, *nr-*
4 *axSpA* non-radiographical axial spondyloarthritis, *ReA* reactive arthritis, *AS* ankylosing spondylitis, *PsA* psoriatic arthritis,
5 *SAPHO syndrome* synovitis acne pustulosis hyperostosis osteitis syndrome.
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 2. Demographic and clinical features of patients with axial Spondyloarthritis.

	axSpA (total group, n=59)	nr-axSpA (n= 49)	AS (n= 10)	P
Age, mean \pm SD years	45.6 \pm 6.1	41.5 \pm 7.5	48.2 \pm 4.7	0.03
Age of onset \pm SD years	38 \pm 4.5	37.2 \pm 5.6	40.1 \pm 6.3	0.27
Male sex	33 (55.9)	27 (55.1)	6 (60.0)	0.45
Symptom duration > 5years	38 (64.4)	18 (36.7)	9 (90.0)	0.02
Clinical features				
Peripheral arthritis	18 (30.5)	16 (32.7)	2 (20.0)	0.23
Enthesitis	13 (22.4)	10 (20.4)	3 (30.0)	0.43
Uveitis	9 (15.5)	6 (12.2)	3 (30.0)	0.22
Psoriasis	1 (1.7)	1 (1.9)	0 (0.0)	
IBD	1 (1.7)	1 (1.9)	0 (0.0)	
BASDAI	42.7 \pm 9.2	39 \pm 11.4	44 \pm 15.5	0.42
BASFI	46.4 \pm 12.9	44.5 \pm 13.8	48.2 \pm 10.2	0.53
ESR (mm/h) median, range	37 (7-110)	36 (7-68)	41 (13-110)	0.40
CRP (mg/L) median, range	22(4-48)	20 (6-48)	26 (6-48)	0.26
<i>axSpA</i> , axial spondyloarthritis, <i>nr-axSpA</i> non-radiographical axial spondyloarthritis, <i>AS</i> ankylosing spondylitis, <i>IBD</i> inflammatory bowel disease.				

Discussion

The prevalence of SpA was 10.7% among rheumatic patients during the 6-month period of the current study and is higher than that found by Malemba and al. (7.5%) based on an extensive review of patients medical records seen by rheumatologists at the UHK. In this hospital-based study, diagnostic criteria applied by rheumatologists were used to improve their clinical diagnosis while just application of the criteria of Amor and ESSG in medical records might lead to misdiagnosis. Moreover, in our environment HLA typing is not feasible and because of the low frequency of HLA B27 also not very well performing. We would state that ESSG and Amor criteria would also need specific validation studies in our region. The issue of HLA B27 mentioned above and the lack of availability of MRI in our regions as well the economic constraints, make the application of the ASAS criteria that heavily rely on this items not feasible as is probably also the case in many other parts of the world. We observed 105 cases of SpA and a male/female sex ratio of 1.4. More men were

1
2
3 affected in the total as confirmed in most of the literature reported from Africa and western
4 countries (18-22). The mean age and the age at the onset of symptom were higher than in the series
5 reported in the western countries, but in agreement with the literature reported from the sub-
6 Saharan region (4, 18-22). A completely different environment (differences in sanitary equipments,
7 differences in infections occurring in these populations) on top of a different genetic background
8 might be responsible for a different disease presentation and perhaps as a consequence also later
9 diagnosis (7). One might overlook specific clinical presentations and as already mentioned classical
10 classification criteria are not validated in this region. It is also necessary to underline the relatively
11 long delay between the onset of symptom and the consultation as found by several African authors,
12 explained mainly by the poverty of population and problems regarding health care in this part of the
13 world (21). The high frequency of endemic infectious diseases in tropical areas and the
14 precariousness of community and individual measures of hygiene would explain the high frequency
15 of ReA. Despite occurring frequently, ReA in our region is expected to present with milder clinical
16 features probably because of a protective role played by the local genetic factors (7, 8). Further
17 genetic research could be interesting in this field. In this study we observed 10 cases of AS (1.0%).
18 This scarcity seems to be related to the low frequency of HLA B27 gene in this population (23). Less
19 male predominance has been observed among Congolese patients with SpA, AS and nr-axSpA
20 compared to Caucasians (3). However different demographical and methodological characteristics
21 could also contribute to the explanations of gender differences observed. The proportion of females
22 could be underestimated because most patients with pelvic inflammatory disease would be seen in
23 Gynecology departments in our country where full rheumatologic evaluations and sacroiliac
24 radiographs are not systematically performed. Patients with AS had a mean age of 48.2 years (SD 4.7)
25 with the age of onset typically older as reported in other sub-Saharan literature and with no family
26 history of SpA and also a relative rarity of extra-articular features, notably uveitis also in accordance
27 with data of the literature of SpA in sub-Saharan Africa (4,6,20-22).

28
29
30
31
32
33
34
35
36
37
38
39
40
41
42 Pertinent differences between AS and nr-axSpA (83.1% of axSpA) in this study included significantly
43 longer disease duration and mean age at consultation for AS ($p < 0.05$). Apart from the fact of AS
44 developing after an initial period of disease with negative radiographical findings, this longer disease
45 duration before consultation can also be explained by the many problems concerning organization of
46 health care, the poverty of the Congolese population having no access to treatment, as well as by
47 cultural specificities with difficulties in understanding the concept of chronicity of a disease (24). No
48 significant difference was observed regarding extra articular features, parameters of disease activity
49 and function as well as inflammatory markers including BASDAI, BASFI, ESR and CRP between these
50 two groups. This is of course difficult to judge in a cross-sectional study of different disease entities
51 when AS might be just the "natural evolution" of nr-axSpA (25-27). Only one case of PsA was
52
53
54
55
56
57
58
59
60

1
2
3 reported in this study in a woman of 32 years' old with HIV negativity. The skin lesions antedated the
4 joint symptoms for three years, including peripheral joint involvement and sacroiliitis. This scarcity of
5 psoriasis and PsA is in accordance with sub-Saharan literature reports (3, 4, 20-22). Further studies
6 must be performed both in Rheumatology and Dermatology to identify case ascertainment of PsA in
7 this spectrum in Congolese population.
8
9

10 **Conclusion**

11 SpA is not rare in outpatients attending Rheumatology units in DR Congo. A population-based study
12 would improve the understanding of this disease spectrum in central Africa. Such a study will need to
13 take into account the differential infectious background, problems related to the health care system
14 and poverty of the population and differential genetics in this environment. Classification criteria
15 validated in the western world will not necessarily perform the same in our region. Also
16 measurements as BASDAI and BASFI should be critically evaluated and compared to specific norm
17 data.
18
19
20
21
22
23

24 **Authors' affiliations**

25
26 1 Rheumatology unit, Department of internal medicine, University Hospital of Kinshasa,
27 Kinshasa, DR Congo

28
29 2 University Hospitals Leuven, Division of Rheumatology, 3000 Leuven, Belgium

30
31 3 KU Leuven, Department of Development and Regeneration, Skeletal Biology and Engineering
32 Research Center, University Hospitals Leuven, Division of Rheumatology, 3000 Leuven, Belgium
33
34

35 **Acknowledgements**

36
37 The authors would like to thank Dr Thierry Lusiense, Department of internal medicine, for helping
38 with acquisition of data from the Rheumatology unit at the Provincial General Hospital of Kinshasa.
39

40 **Contributors**

41 PL wrote protocol, recruited and enrolled participants, collected data, and drafted the report. JMM
42 analyzed and interpreted the data. JMM served as experienced rheumatologist, participated in the
43 design and helped to draft the manuscript. KDV and RW helped interpreting data, writing and edited
44 the final version of the manuscript. PL had full responsibility for the integrity of the data and the
45 accuracy of the data analysis.
46
47
48
49
50
51

52 **Funding:** This research did not received any specific grant from any funding agency from the public,
53 commercial or not-for-profit sectors

54 **Competing interests:** None declared.
55
56
57
58
59
60

1
2
3 **Patients' consent:** Obtained.

4 **Ethics approval:** National Ethic Committee (ESP/CE/030/13).

5
6 **Data sharing statement:** Extra data can be accessed via the Dryad data repository at DOI:

7
8 doi:10.5061/dryad.0n5f66n
9

10
11
12 **References**
13

- 14 1. Sieper J, Rudwaleit M, Khan MA, Braun J (2006) Concepts and epidemiology of
15 spondyloarthritis. *Best Pract Res Clin Rheumatol* 20:401–17
- 16 2. Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, et al (2009) The
17 development of Assessment of SpondyloArthritis international Society classification criteria
18 for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 68:777–83
- 19 3. Stolwijk C, van Onna M, Boonen A, van Tubergen A (2015) Global Prevalence of
20 Spondyloarthritis: A Systematic Review and Meta-Regression Analysis. *Arthritis Care Res*
21 (Hoboken) Dec 29
- 22 4. Tikly M, Njobvu P, McGill P (2014) Spondyloarthritis in Sub-Saharan Africa. *Curr Rheumatol*
23 *Rep* 16:421
- 24 5. Rachid B, El Zorkany B, Youseif E, Tikly M (2012) Early diagnosis and treatment of ankylosing
25 spondylitis in Africa and the Middle East. *Clin Rheumatol* 31:1633–9
- 26 6. Mijiyawa M, Oniankitan O, Khan MA (2000) Spondyloarthropathies in sub-Saharan Africa.
27 *Curr Opin Rheumatol* 12:281–6
- 28 7. Cao K, Moormann AM, Lyke KE, et al (2004) Differentiation between African populations is
29 evidenced by the diversity of alleles and haplotypes of HLA class I loci. *Tissue*
30 *Antigens* 63:293–325
- 31 8. Mathieu A, Paladini F, Vacca A, Cauli A, Fiorillo MT, Sorrentino R (2009) The interplay
32 between the geographic distribution of HLA-B27 alleles and their role in infectious and
33 autoimmune diseases: A unifying hypothesis. *Autoimmun Rev* 8:420-5
- 34 9. Brown MA, Jepson A, Young A, Whittle HC, Greenwood BM, Wordsworth BP (1997)
35 Ankylosing spondylitis in West Africans—evidence for a non-HLA-B27 protective effect. *Ann*
36 *Rheum Dis* 56(1):68–70
- 37 10. Solomon L, Beighton P, Valkenburg HA, Robin G, Soskolne CL (1975) Rheumatic disorders in
38 the South African Negro. Part I. Rheumatoid arthritis and ankylosing spondylitis. *S Afr Med J*
39 49(32):1292–6

- 1
- 2
- 3 11. Díaz-Peña R, Blanco-Gelaz MA, Njobvu P, López-Vazquez A, Suárez-Alvarez B, López-Larrea C
- 4 (2008) Influence of HLA-B*5703 and HLA-B*1403 on Susceptibility to Spondyloarthropathies
- 5 in the Zambian Population. *J Rheumatol*35(11):2236-40
- 6
- 7 12. Singwe-Ngandeu M, Meli J, Ntsiba H, Nouedoui C, Yollo AV, Sida MB, et al (2007) Rheumatic
- 8 diseases in patients attending a clinic at a referral hospital in Yaoundé, Cameroon. *East Afr*
- 9 *Med J* 84(9):404–9
- 10
- 11 13. Malemba JJ, Mbuyi-Muamba JM (2008) Clinical and epidemiological features of rheumatic
- 12 diseases in patients attending the university hospital in Kinshasa. *Clin Rheumatol* 27:47–54
- 13
- 14 14. Rudwaleit M, Landewé R, van der Heijde D, Listing J, Brandt J, Braun J, et al (2009) The
- 15 development of Assessment of SpondyloArthritis international Society classification criteria
- 16 for axial spondyloarthritis (part I): classification of paper patients by expert opinion including
- 17 uncertainty appraisal. *Ann Rheum Dis* 68: 770–6
- 18
- 19 15. Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, et al (2009) The
- 20 development of Assessment of SpondyloArthritis international Society classification criteria
- 21 for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 68: 777–83
- 22
- 23 16. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H (2006) Classification
- 24 criteria for psoriatic arthritis: development of new criteria from a large international study.
- 25 *Arthr & Rheum* 54: 2665-73
- 26
- 27 17. Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P, Jenkinson T (1994) A new
- 28 approach to defining functional ability in ankylosing spondylitis: the development of the Bath
- 29 Ankylosing Spondylitis Functional Index. *J Rheumatol*21(12):2281-5
- 30
- 31 18. Dean LE, Jones GT, MacDonald AG, Downham C, Sturrock RD, Macfarlane GJ (2014) Global
- 32 prevalence of ankylosing spondylitis. *Rheumatology* 53:650-7
- 33
- 34 19. Usenbo A, Kramer V, Young T, Musekiwa A (2015) Prevalence of Arthritis in Africa: A
- 35 Systematic Review and Meta-Analysis. *PLoS One* 10(8):e0133858
- 36
- 37 20. Mijiyawa M, Oniankitan O, Khan MA (2000) Spondyloarthropathies in sub-Saharan Africa.
- 38 *Curr Opin Rheumatol* 12(4):281-6
- 39
- 40 21. Belachew DA, Sandu N, Schaller B, Guta Z (2009) Ankylosing spondylitis in sub-Saharan Africa.
- 41 *Postgrad Med J* 85(1005):353-7
- 42
- 43 22. Ouédraogo DD, Meyer O (2012) Psoriatic arthritis in Sub-Saharan Africa. *Joint Bone Spine*
- 44 79(1):17-9
- 45
- 46 23. Mbayo K, Mbuyi-Muamba JM, Lurhuma AZ, Halle L, Kaplan C, Dequeker J (1998)Low
- 47 frequency of HLA-B27 and scarcity of ankylosing spondylitis in a Zairean Bantu population.
- 48 *Clin Rheumatol*17(4):309-10
- 49
- 50
- 51
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

- 1
2
3 24. Lebughe LP, Malemba JJ, Divengi JP, Mbuyi-Muamba JM (2016) Itineraries of the rheumatic
4 patients towards the rheumatologist in DR Congo. *Afr J Rheumatol* 4(2): 63-65
5
6 25. Kiltz U, Baraliakos X, Karakostas P, Igelmann M, Kalthoff L, Klink C et al (2012) Do patients
7 with non-radiographic axial spondylarthritis differ from patients with ankylosing spondylitis?
8 *Arthritis Care Res* 64(9):1415-22
9
10 26. Malaviya AN, Kalyani A, Rawat R, Gogia SB (2015) Comparison of patients with ankylosing
11 spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) from a single
12 rheumatology clinic in New Delhi. *Int J Rheum Dis* 18(7):736-41
13
14 27. Burgos-Varga R, Wei JC, Rahman MU, Akkoc N, Haq SA, Hammoudeh M et al (2016) The
15 prevalence and clinical characteristics of non-radiographic axial spondyloarthritis among
16 patients with inflammatory back pain in rheumatology practices: a multinational, multicenter
17
18
19
20 18(1):132
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60