PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Spondyloarthritis in the Democratic Republic of Congo: a prospective hospital-based study
AUTHORS	Lebughe, Pierrot; de Vlam, Kurt; Westhovens, Rene; Mbuyi-Muamba, Jean-Marie; Malemba, Jean Jacques

VERSION 1 – REVIEW

REVIEWER	Ade Adebajo University of Sheffield Medical School Faculty of Medicine, Dentistry and Health Beech Hill Road S10 2RX United Kingdom
REVIEW RETURNED	01-Dec-2017

GENERAL COMMENTS	This study provides the most comprehensive and up to date study of Spondyloarthropathies in Sub-Saharan Africa. I am still unclear as to why HLA genotyping was not performed. Are there normal metrology values for the African population studied (for spinal measurements, BASFI etc) so as to compare abnormal values with. What is the prevalence of HIV in the region, in view of previous reports of a strong association between HIV and spondyloarthropathies in Sub-Saharan Africa. In addition, what is the prevalence of sexually transmitted infections such as Chlamydia, in the region and does this also influence the study findings. What criteria was used for the diagnosis of juvenile spondyloarthritis. Coud the acute phase responses noted, be as a result of chronic infection rather than from inflammation associated with spondyloarthritis.

REVIEWER	Carmen Stolwijk Department of rheumatology, Franciscus gasthuis Rotterdam, the Netherlands
REVIEW RETURNED	06-Dec-2017

GENERAL COMMENTS	This is an interesting study about the prevalence of SpA and its

	subtypes in the republic of Congo. There are only a few studies about SpA in sub-saharan Africa, and therefore, this study adds useful in information. The introduction and objective of the study is clear. I have some minor comments: Methods section: - was this study performed retrospectively from medical records? Please clarify. - the section about the classification criteria is a bit confusing for me. First, the authors state that patients are diagnosed according to the Amor and ESSG criteria or a clinical diagnosis. Why were these criteria used and not the ASAS criteria? Second, the authors describe the axiale SpA and CASPAR criteria. Please specify. Results: - how did the patients came into the rheumatology unit? were they referred by a GP? - how many of the 105 patients were diagnosed according to the amor or ESSG criteria and how many on clinical grounds? - please be consistent in the number of decimals used. Discussion: - it is important to mention that classification criteria are not meant for diagnosis of patients. Do you think any patients do fulfill the criteria but do not have SpA? - MRI is also part of the axial SpA criteria. Is there access to MRI in Congo? - please add strengths and limitations

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 (Ade Adebajo)

1/I am still unclear as to why HLA genotyping was not performed?

Answer: HLA typing is available in Kinshasa only since one year, so it could not be performed during the current study. Moreover, economic restraints in a difficult health care environment would make it very difficult without specific funding. In future research we will try to find specific funding for this as this study is only the first of a more global initiative trying to understand spondyloarthritis in central Africa. All this is now specified in the manuscript.

2/ Are there normal metrology values for the African population studied (for spinal measurements, BASFI etc) so as to compare abnormal values with?

Answer: We have not found data concerning normal metrology values for Africans in the literature. So, comparison was not possible at this moments; we will do so in future studies. We mentioned in conclusions the need for critically evaluating these measurements in the Congolese population in the future.

3/What is the prevalence of HIV in the region, in view of previous reports of a strong association between HIV and spondyloarthropathies in Sub-Saharan Africa?

4/In addition, what is the prevalence of sexually transmitted infections such as Chlamydia, in the region and does this also influence the study findings?

Answers: 3/ and 4/ Currently the prevalence of HIV/AIDS in the DR Congo is 1.2%, according to the report of UNAIDS/DRC (2016). The association between HIV and Spondyloarthritis was not looked for in the present study. The same holds for the prevalence of other sexually transmitted infections. This is now added to the limitations of this study.

5/ What criteria were used for the diagnosis of juvenile spondyloarthritis?

Answer: Juvenile spondyloarthritis was diagnosed in patients with spondyloarthritis (axial or peripheral spondyloarthritis or enthesitis related arthritis) which began before the age of 16 and persisted more than 6 weeks.

6/ Could the acute phase responses noted, be as a result of chronic infection rather than from inflammation associated with spondyloarthritis?
Answer: We can't confirm that the acute phase response noted was due to a chronic infection although an absolute statement will be difficult on this issue. All patients were in clinical follow up and active clinical infections were not noted at the moment of inclusion.

Reviewer 2 (Carmen Stolwijk)
1/ was this study performed retrospectively from medical records? Please clarify.
Answer: This study was performed prospectively. Patients were consecutively recruited among rheumatic patients who attended the rheumatology units of 2 hospitals of Kinshasa . This is now clarified in the manuscript.
2/ - the section about the classification criteria is a bit confusing for me. First, the authors state that patients are diagnosed according to the Amor and ESSG criteria or a clinical diagnosis. Why were these criteria used and not the ASAS criteria? Second, the authors describe the axial SpA and CASPAR criteria. Please specify.
Answer: The ASAS classification criteria were not used because HLA typing was not available and also MRI was available only in one hospital. Moreover in a difficult health care environment without reimbursement system, in a country with serious economic problems, these key elements of the ASAS classification are not feasible as in probably many other countries of the third world. So it was not possible to use these criteria in this study. The generalizability of these criteria may be questioned since they need more sophisticated tools which are not worldwide accessible for many patients. Moreover due to important local conditions must be validated separatedly, given the different infectious background, low prevalence of HLA B27 etc. Axial spondyloarthritis was defined in patients with predominantly axial symptoms with or without peripheral manifestations, while peripheral spondyloarthritis were applied in patients with predominantly symptoms of arthritis, enthesitis or dactylitis. The CASPAR criteria were applied in patient with Psoriatic arthritis.
3/how did the patients came into the rheumatology unit? were they referred by a GP?
Answer: Some patients (30%) were referred by general practitioners, but the majority came directly to the hospital. It must be noted that health care organization and the health system is different from that in the developed world.
4/- how many of the 105 patients were diagnosed according to the Amor or ESSG criteria and how many on clinical grounds?
Answer: 78 patients were diagnosed according to the Amor or ESSG criteria and 27 patients were diagnosed according to clinical grounds based on the rheumatologist experience. This is now added to the text.
5/ please be consistent in the number of decimals used.
Answer: We have this corrections in the manuscript.
6/ it is important to mention that classification criteria are not meant for diagnosis of patients. Do you think any patients do fulfill the criteria but do not have SpA?
Answer: We fully agree. In this daily practice study, diagnosis was based on clinical findings. Secondarily, the classification criteria (Amor, ESSG) were applied in these patients.
7/ MRI is also part of the axial SpA criteria. Is there access to MRI in Congo?
Answer: cfr the answer to reviewer 1. There is availability in one hospital but due to economic problems MRI is not really feasible. Moreover one could raise some critical thoughts using MRI in a population practicing heavy work with an important load to the lower back. We refer to: Varkas G, de Hooge M, Renson T et al. Effect of mechanical stress on magnetic resonance imaging of the sacroiliac joints: assessment of military recruits by magnetic resonance imaging study. Rheumatology (Oxford). 2017 Dec 14. doi: 10.1093/rheumatology/kex491. [Epub ahead of print]
This research group intends to start research into spondyloarthritis in central Africa with an open mind, not just copying what is done in the Western world.
8/ and please add strengths limitations.
Answer: We made some corrections in the manuscript and added some limitation.

VERSION 2 – REVIEW

REVIEWER	Carmen Stolwijk Franciscus Gasthuis Rotterdam
REVIEW RETURNED	05-Feb-2018

GENERAL COMMENTS	I am happy with the corrections The term Reiters disease is no longer used