Reviewer's report

Title: CD64 as a biomarker in septic arthritis

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Reviewer: Saul Faust

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1. Is the question posed by the authors well defined?
   The question is well defined: does CD64 distinguish different clinical phenotypes in acute arthritis? As CD64 has been proposed as a discriminatory biomarker, this is a useful question.

2. Are the methods appropriate and well described?
   Methods were appropriate with healthy and chronic disease controls. However, the cases included/excluded in group 4 are not clearly defined in terms of timescale or how this would affect the potential use as a clinical diagnostic marker. For example, 8 (of 69) were excluded from the analysis due to “uncertain final diagnosis” and 4 (of 69) subsequently recovered without antimicrobials so were analysed in group 3. From a clinical use perspective, this means the data appear stronger for CD64 than they would otherwise do – to be useful the data might have been better chosen as the “69 presenting with acute arthritis”. Only 26 had culture proven infection of whom only 12 had positive blood cultures (not an unusual situation in bone and joint infections where definitive microbiological diagnosis is commonly unproven in clinical practice without novel molecular diagnostics being used). 7 of the “included infections” lacked CD64 analysis.

3. Are the data sound?
   The data appear to be sound.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   It is not stated where the data are to be deposited. The tables are clear and detailed for the septic arthritis cases detailed.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   The discussion is balanced and explains clearly that CD64 is increased in patients with septic arthritis compared to other forms of arthritis. However, the sensitivity is low and it is not useful to rule out infection where the marker is not raised. CRP is stated as “proved to have the best diagnostic accuracy as measured by AUC”.
   The discussion further goes on to explain that CD64 is predominantly raised in cases with positive blood cultures but not in localised infection.
   However, the conclusions are perhaps too much in favour of CD64 as a potential
clinically useful biomarker. From a clinical perspective, the new flow cytometry based test (CD64) under investigation has not been demonstrated to be of any great benefit compared to routinely available and cheap biomarkers (eg CRP), or potentially useful others (eg procalcitonin) especially due to the major limitation described: lack of sensitivity in localised infection.

6. Are limitations of the work clearly stated?
The discussion describes the range of pathogens (gram positive, low virulence, negative blood culture) as potential difference to previous studies but in fact this is likely to be the case in pragmatic “real life.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes

8. Do the title and abstract accurately convey what has been found? Yes

9. Is the writing acceptable? Yes

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No