Author's response to reviews

Title: Tuberculosis Lymphadenitis Diagnosis in children Using Fine Needle Aspiration in Bangui

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Response to the reviewer’s report

**Reviewer:** David Alexander

**Major compulsory revisions:**

Line 108: How many cases had 1 node sampled and how many had 2? Were both nodes sampled with a single needle, or were separate FNAs performed, stained and cultured for each node? If separate FNAs were performed for each node, were more than 131 samples assessed? Among cases with 2 FNAs, how many were discordant (e.g. 1 node TB positive, 1 node negative).

34 children had single node and 97 had multiple nodes. FNA was done using a different needle. AFB and cultures were done on all specimens from each patient. Patients were diagnosed as positive for TB when one or several lymph nodes gave positive results to TB identification. Unfortunetly the software used for the database of diagnostic results obtained with FNA does not allow to associate the data with individual patients. Therefore we could get only a global idea of the efficiency of the diagnosis performed either on single nodes or multiple nodes.

Line 109: Was the positivity rate equivalent for both groups – or did sampling 2 lymph nodes improve detection?

We added in the result section (line 104) this sentence: “among positive ZN patients 49.5% presented multiples nodes against 23.5% in patients with single node (0.01)”.

**Title/Authors Affiliations:** Define ‘RCA’. Similarly, both RCA and CAR are used in the manuscript. For consistency, pick one for use throughout the paper.

**Corrected:** we changed RCA by CAR in the manuscript

In Line 120, the authors correctly state that ‘culture is the gold standard method for detection of tubercle bacilli’. However, in line 124, they suggest that ‘The gold standard test for a definitive diagnosis is certainly a lymph node biopsy’. Although biopsy may be the recommended or preferred method for obtaining a sample for testing, it is not a gold standard for diagnosis of TB.

**Corrected in the discussion:** line 136
Table 4 does not provide counts for bacillary loads, just the proportions of culture positive/negative and HIV positive/negative cases. Also, it seems counterintuitive that patients with intact immune systems would have higher bacillary loads than the immunocompromised. Please explain and/or provide references.

This is not counter intuitive. The bacilli are replicating in macrophagis. Due to immunodepression, less macrophagis might be present at the site of infection and therefore less bacilli could replicate.

‘This’ can be explained by a lower bacillary load in lymph nodes of immune-compromised patients. This sentence is deleted

Lines 150-153: Include references (e.g. 19 & 20) describing the efficacy of NAAT with FNA.

Included

Lines 159-160: In ref 19, the sensitivity of the Xpert MTB/RIF assay was 64% (89/138) for smear-negative cases. In the current manuscript, Table 2 indicates that the sensitivity of culture was 67% (49/73) for smear-negative cases. Although NAAT may be effective with AFB positive samples, it may not ‘improve the overall diagnostic sensitivity of FNA.’

Corrected

Discretionary Revisions

Lines 133-134: Could the AFB positive/culture negative samples from untreated patients represent infections with non-tuberculous mycobacteria (NTM) that do not grow on the media and/or incubation temperatures used in this study? In Bangui, how common are NTM infections?

The AFB positive/culture negative samples are from patients who are previously treated. NTM infections are very rare in CAR.

Lines 148-165: Consider removing, or at least shortening, the discussion of NAAT and the GeneXpert MTB/RIF assay. The technique is not used in the current manuscript and it seems incongruous to promote NAAT in a manuscript where the stated objective is to evaluate the efficacy of FNA.
The sentence included in the discussion is not a promotion of any kind of commercial test. We have modified it. However, because the diagnosis of tuberculosis is a bacteriologic diagnosis, any improvement of the detection of the bacilli or part of it (nucleic acid) will improve the diagnosis. Therefore we prefer to keep this sentence in the discussion.

Tables 2 and 4: Consider combining these into a single table that includes data for culture, microscopy and HIV serology results. Alternatively, eliminate Table 4 and discuss the statistics in the text.

In general, the manuscript reads well. However, the current draft includes numerous grammatical errors and some unusual expressions. These should be corrected. Some examples include:

Title: Fine Needle Aspiration for the Diagnosis of Tuberculosis Lymphadenitis in Children from Bangui

The title has been changed:

Tuberculosis Lymphadenitis Diagnosis in children using Fine Needle Aspiration in Bangui has been changed by Fine Needle Aspiration for the Diagnosis of Tuberculosis Lymphadenitis in Children from Bangui

Line 46: replace ‘tribute’ with ‘price’ or ‘toll’

Corrected

Line 79: replace ‘research’ with ‘detection’ or ‘visualization’

Corrected

Line 86: replace ‘indirect method of proportions’ with ‘indirect proportion method’

Corrected

Line 116: replace ‘not exploitable due to contaminations.’ with ‘excluded due to contamination.’

Corrected
Reviewer: Ian Kitai

The definition of lymphadentitis (line 99) should appear in the methods section (not results)

Corrected

Was there specific positioning used for different groups? In general who held the child- if known-

In general parents or guardians held the child

What size of syringe was used? A 18 G needle (1.2 x 40mm) was used.

What happened to the material- was some placed on a slide and fixed, or was all sent for culture. What was sent- material in a separate container (what type of container), or the needle and syringe?

Only the needle and syringe were sent to the “Institut Pasteur de Bangui”.

Is there an estimate of the delay between aspiration and inoculation? Was addressing applied after? This is important for those who may decide to use this method.

ZN staining was done automatically, then inoculation on LJ medium.

If more than one node was sampled was this using a different needle or the same needle?

Different needle was used for each node: one needle for each node.

The methods section does not include the type of microscopy used. The discussion, it mentioned LED microscopy but was this case for these patients?

After ZN staining, optic microscopy was used.

Results section:

In the result section, it is unclear which node(s) was/were sampled (in comparison to the node/s which the child was said to have presented with). These data may not be in available and don’t preclude publication but they are important if present.

All children aged 0-17 years addressed at Unit D in the paediatric hospital with lymph nodes in various locations, evolving for over one month with an unknown etiology, were included.
The safety of the procedure is important. There is no mention of any complications such as hemorrhage or secondary infection or the development of sinuses. Were these explicitly assessed? Were any side effects found passively. These may not have been monitored: this should be acknowledged as it could be an issue that needs further study.

Complications such as hemorrhage or secondary infection or the development of sinuses were not assessed because we don’t have feed-back from clinician about an eventual complication. This aspect should be considered for further studies.

In addition, the procedure is said to be suitable for use by nurses in clinics, but is unclear who performed the test in this study.

It is added: line 76