Author's response to reviews

Title: Useful Clinical Features and Hematological Parameters for the Diagnosis of Dengue Infection in Patients with Acute Febrile Illness: A Retrospective Study

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Dear Editor and reviewers,

Reference number: BHEM-D-18-00009 and BHEM-D-17-00018

Thank you for your letter and constructive comments concerning our manuscript entitled “Useful Clinical Features and Hematological Parameters for the Diagnosis of Dengue Infection in Patients with Acute Febrile Illness: A Retrospective Study: Reference number: BHEM-D-18-00009 and BHEM-D-17-00018”. We studied your comments carefully and made corrections
with track change which we hope to meet with your approval. We answered your questions and comments in details in the following texts.

Replies to questions and comments:

Answer to Reviewer 1;

Comment 1: This is a retrospective study where I have the impression is that selection of patients was based on microbiological diagnosis and not on clinical presentation. The latter is however suggested.

Reply: Thank you for your concern in this point. We already clarify this issue in our manuscript as your suggestion. The selection was initially based on clinical presentation, then was confirmed by microbiological diagnosis.

“The inclusion criteria were patient with acute febrile illness (less than 7 days) without any identified source of infection. Patients must have had serology test or blood culture to confirm the diagnosis to be included in the study.”

(Method part, page 9, line 14-16).

Comment 2: It is unclear how many of the dengue patients were NS1 positive and how many IgM Dengue pos. There is no indication which tests were used although there may be large variation in sensitivity and specificity.

Reply: Thank you for this important comment.

According to this comment, we have changed our result part to answer this question.
“The serologic result for dengue group was positive for NS1 antigen in 57.79% (89/154), dengue IgM antibody in 27.92% (43/154) and both in 14.29% (22/154).”

Both test has high sensitivity on different day of fever. The decision was based on physician decision and also with patient presentation and day of fever.

(Result part, page 11, line 10-12)

Comment 3: Unclear is whether only inpatients were included or also out-patients?? Possibly the patients with bacteria infection were much more sick (all admitted) and recovered much slower compared to Dengue (also out-patients?), possibly contributing to persistent differences in CBC in patients groups.

Reply: Thank you for this necessary question and important concern for this issue. We recruit patient from both inpatient and outpatient. We change in the method part as follow to clarify this issue.

“We retrospectively reviewed medical records of patients age 15 years or older who presented at Chiang Mai University Hospital for both inpatient and outpatient between September 2013 and July 2015.”

(Method part, page 9, line 12-14)

Comment 4: Exclusion criteria were, among others platelets less than 140.000 or more than 40.000: this is very unclear to me as low platelets numbers are a feature of dengue virus infection.

Reply: Thank you very much for this informative question.
For this point of view, we intended to exclude the patient who had cytopenia from underlying disease or other previously causes. This will help us to determine that the differences of CBC was caused from infection. This was already documented in our method part.

“This study excluded patients with previously documented anemia (Hb less than 13 g/dl in men, 12 g/dl in women or mean corpuscular volume (MCV) value outside the range 80-100 fl), WBC count less than 5000 per cu.mm., platelet count less than 140,000 or more than 400,000 per cu.mm”

(Result part, page 9, line 22-25).

Comment 5: Statistics are unclear as an estimated prevalence of 20% was indicated, but of what is not indicated.

Reply: Thank you very much for your concern.

We use the W.G. Cochran formula to calculate the sample size of this study. The prevalence of 20% was from the following paper that stated the prevalence of dengue infection is around 19-20% from patient who presented with fever.


We explain this in the method part as followed.

“The sample size was calculated using the formula N = P × (100 - P) × z2/d2 in which P was the anticipated prevalence, d was the desired precision and z was the appropriate value from the normal distribution for the desired confidence. We estimated an anticipated prevalence of 20% with 95% confidence (Z=1.96) of achieving a precision of 10%. The calculated sample size was 300 patients, divided in to 2 groups; the dengu group and control group.”

(Method part, page 10, line 4-9).
Comment 6: Procedures of blood sampling is unclear: first sample at presentation to facility or during admission? Frequency of blood taking was according to physician. How many patients were taken blood only once, or twice?? CBC results are related to days of fever: not described in methods.

Reply: Thank you very much for this important point. We change this concern in our method part as followed.

“The CBC parameters were collected every time the blood test was performed related to days of fever until disease recovery at tenth day”

(Method part, page 10, line 20-21).

Since the patient was recruited from both inpatient and outpatient, the first blood sample can be collected from both at presentation to facility or during admission.

In table 3, we showed CBC parameters of dengue and control groups by day of fever.

The median time of blood test was 3 times (minimum 1 time and maximum 8 times).

Only, 18 patients have 1 time of blood test and 32 patients have 2 times of blood test.

Comment 7: The presented clinical and laboratory results (high hematocrit, thrombopenia, leucopenia, atypical lymphocytes, monocytosis etc) in Dengue have been described in literature before.

Reply: Thank you very much on your concern in this point.
We totally agree with your concern. But in our study which were different from previous study, we identified important clinical presentations and the changes in all comprehensive CBC parameters on each successive day of the fever, also compared with the control group.

Answer to Reviewer 2;

Comment 1: Table 1 and Table 3. Remove the percent sign in each data because the header of the column is specified.

Reply: Thank you very much for your concern and informative suggestion.

We have deleted the percent sign in all data in Table 1 and Table 3 as per track change in the attached table file.

We really hope these modifications can meet with your approval. Thank you very much.

Yours Sincerely,

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