Author's response to reviews

Title: Community acquired bacterial meningitis in Cuba: a follow up of a decade.

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COVER LETTER ADDRESSING RESPONSE TO REVIEWER

EDITORIAL REQUEST

About ethical approval of our research, we should say that it is a follow up study (not an experimental or quasiexperimental research) with data source resulting from the nationwide surveillance system. Therefore, we clarify this issue in material and method section as follows:

“The present study did not require approval from an Ethics Committee. The Cuban Ministry of Public Health is the governmental organization responsible for the collection of infectious disease notifications, hospital discharge records and population or laboratory surveillance. The management of these data for public health purposes does not require a patient's informed consent nor does it require any authorization regarding privacy laws in Cuba”

RESPONSE TO THE REVIEWERS

We are grateful to reviewers for their helpful comments and suggestions which we try hard to clarify in this document, as well as in the paper.

First Reviewer
Version: 1 Date: 14 September 2009
Reviewer: Annunziata Faustini
Reviewer’s report:

RESPONSE

We try to improve the redaction and better define the aims of the study, for a better understanding of the analytical method used. This research is based on a surveillance system implemented as a part of the infectious neurological syndrome national program for control and prevention, in which are included all causative bacteria and, contrarily to other surveillance, include complementary information about patients regarding to clinical features, date of symptoms onset, medical consultation, hospitalisation and decease, also attendance to day care,
boarding school, occupational categories, vaccination status, crowding in dormitories, hot bed control and microbiological findings. We did not include all this information in a single paper because it may be result overloaded.

THE AIMS OF THE PAPER

As we said above, we better defined the aims, which are two: 1. to characterize the main epidemiological features of BM and 2. To assess the association with mortality of some variables reported by surveillance, therefore, there was no a third aim related with evaluating the surveillance impact or the effectiveness of the enhanced BM surveillance in Cuba. When we said at the end of background section: “to explain the Cuban experience in surveillance of this group of diseases “, we simply refer to share our experience through the results we presented. Perhaps it was miswritten or misunderstood.

However, we attempt, after reading the reviewer comments, to better describe the surveillance characteristics in background and material and methods. When we say integrated surveillance is because information from different areas (demographic, epidemiology, medical care, microbiology) was synthesized in a single questionnaire and this characteristic enhance or improve the results as well as the epidemiological analysis.

The analysis of factors associated to mortality was on the basis of a logistic regression for some variables (age, gender, children at home, children at DCC, day students, boarding students, housewife, pensioned, military, imprisoned, unemployed and causal agents N. meningitidis, S. pneumoniae, Hib, non-identified bacteria and other isolated) with RR>1.3 in previous bivariated analysis. The model was fitted including all the above mentioned exploratory variables and subsequently dropped one by one until only those that were associated (OR>1.8).

ANALYSIS OF TREND AND ITS CAUSES

Reviewer suggest a formal analysis for trend should be carried out to take into account the annual variability of the rates, and for that reason we made an analysis trend by polynomial model including morbidity and mortality. Previously only a linear trend analysis for morbidity was made.

With regard to the important role of vaccination campaigns with VA-MENGOC BC® and against Hib (which is also produced in Cuba since 2004) in reducing incidence, we better describe and discuss the vaccination campaigns and program which are much extensively described in the bibliography.

According to our experience low morbidity must be due to prevention strategy, and also considering the herd immunity achieved in the population. High mortality in the elderly may be mainly related with poor and untimely recognition of symptoms, but other factors regarding medical attendance (and not included in the present study) as well as underlying conditions and virulence of bacteria, as appear in DISCUSSION.

GEOGRAPHICAL DISTRIBUTION

For the geographical analysis we based on the distribution of the incidence at
provincial level from available surveillance data. Vaccination coverage achieved and health services are very similar along the country and no important differences in central provinces compared with other has been found. Solar radiation and climate variation are more likely influencing high incidence in that region and we include in discussion an explaining reference. Studies of geographical distribution of the pathogenic bacteria are undergoing and results are not available yet.

RISK FACTORS
As we above mentioned age and gender and pathogenic bacteria were included in regression analysis for mortality and were described more efficiently after the suggestion of reviewer.

We agree with reviewer that a multivariable approach is essential in estimating the strength of the association, to control the confounding effects of the other variables and to assess the interaction between variables.

BM of unknown aetiology was included in analysis of factors associated to mortality and compared to those of known aetiology.

With regard to personal curiosity of reviewer about why the authors did not analyse the total time lapse from symptoms onset to hospitalization, we can say that we did the analysis but did not show association with mortality, therefore having the information of both period it seems to us more likely to find an association separately. We must say that in Cuba, the start of the therapy is at the moment when patient is admitted at hospital, according to the recommendation of the infectious neurological syndrome national program for control and prevention.

DISCUSSION
Reviewer raise the issue of discussion of incidence data presented in the paper and we try to explain the temporal variations trends of incidence and mortality, as well as the monthly distribution taking into account all variables under surveillance.

Climatic differences are discussed from the scope of previous studies in Cuba linking the increased incidence in that region with socioeconomic factors and climatic variations.

MINOR POINTS
Regarding the age groups for infants and children we used, in Cuba are correspondent with the main educational levels (1-5 yrs Day Care Centres, 6-11 yrs Primary School, 12-14 yrs Secondary Basic School) which are known as risk factors for respiratory transmission diseases.

Regarding information bias, we clarify in material and methods that the information was obtained by epidemiologists which interviewed patients and their relatives in successive sessions at hospital and home, as a part of the hot bed control.
Comments: The objective of the study seems quite highlighted and the methods used are appropriate and well described. The discussion and conclusions are balanced and adequately supported by the data. The authors appropriately attempted to discuss the limitation of the study. The references are recent and fitting.

The reviewer did not raise any concern to be explained by authors.