Author's response to reviews

Title: Genotype distribution of human papillomavirus (HPV) in histological sections of cervical intraepithelial neoplasia and invasive cervical carcinoma in Madrid, Spain.

Authors:

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Author's response to reviews: see over
Dear Sir:

Please find hereby attached for your consideration the review of our work entitled “Genotype distribution of human papillomavirus (HPV) in histological sections of cervical intraepithelial neoplasia and invasive cervical carcinoma in Madrid, Spain.”

Answers to the reviewer and changes made in the manuscript:

A.A1: Added, done as reference number 3. All references from the number 3 have been renumbered

R1.Q2: Your study is NOT longitudinal. A longitudinal study implies that subjects in the study are seen more than once to follow-up on their status. YOUR STUDY is a cross-sectional study. Please revise.
A.A2: Revised

R1.Q3: I am still not sure about what you mean regarding the selection of samples….You stated “…total of 1,137 abnormal specimens from fixed tissue sections of biopsies and LEEPs diagnosed since January 2005 to July 2010 were included, as a consecutively stratified not randomly taken samples” Do you mean that you take all samples from 2005 and 2011. If yes, why don’t you just simplify and state that you selected all samples diagnosis between 2005 and 2011….
A.A3: Changed as: “This is a cross-sectional and retrospective study, in which all cases diagnosed between January 2005 and July 2011 (1,137 abnormal specimens from fixed tissue sections of biopsies and LEEPs) were selected.”

R1.Q4: Authors did not answer previous comment about providing 95% confidence intervals for estimates (percentage). I strongly believe that this should be included.
The Method section should provide the details about the analysis. For example, different methods were used to estimate % in tables 2 and 4. This should be explained. 95% confidence intervals should also be provided for estimates (percentage).
A.Q4: Done. Added 95%CI in the tables 2 and 4.
R1.Q5: The Result section (and other portion of the manuscript) are still written as an output and not as a manuscript.
A.Q5: We consider it necessary to specify each of the results as we have done in order to the rigor of the data.

R1.Q6: The Discussion is well written. However, results should be discussed and compared considering 95% confidence intervals around their estimates. For example, authors concluded that HPV18 was more prevalent in CIN1 (7.2%) than in CIN 2-3 (5.7%). Authors need to be cautious when comparing similar results. CIs probably do not differ (no significant difference).
A.Q6: Done.

R1.Q7: Conclusion can be merged with the Discussion. And the last sentence of the conclusion is very strong.
A.Q7: Done and changed.

R1.Q8: Important limitations of the study should be discussed: Small sample size; Low external validity (only one site), hard to generalize the results to the entire population of Spain; Detection of only 20 HPVs genotypes whereas more than 40 mucosal exist. It may underestimate HPV prevalence etc.
A.Q8: We added a final section in the discussion under the heading "Weaknesses of the study:
Our study presents some limitations. First, the origin of the samples from only one hospital may do hard to generalize the results to the entire population of Spain. However, this hospital is a reference centre in which patients of many places of the Region of Madrid are attended. Also, the results obtained in this study agree with data about population located in other Spanish regions and previously published.

Second, whereas more than 40 anogenital HPV types exist, only 20 were detected in this study. But all the HPVs genotypes usually implicated in the origin of the cervical cancer are detected.

Third, the small sample size of benign lesions and ICC affect to the study’s significance. However, the difficulty to obtain ICC cases in Spain gives value to these results. In the future, it would be of interest to obtain more cases for further studies.”

The work now consist of 14 pages and 4 tables (abstract included). Our current address, telephone and fax number are:

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We thank you for your attention and remain expectant for your response.

Yours faithfully,

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