3th Jul 2016

Dear Editor,

We would like to thank you for the acceptance of our manuscript in the prestigious journal of "World Journal of Gastroenterology". Please find our revised manuscript entitled "**Incidence, clinical features and Para clinical findings of achalasia in Algeria: experience of 25 years**." under Ref. ESPS manuscript NO: 26246. Please note that we publish this article as an "original paper". We would like to warmly thank the reviewers for their pertinent remarks and suggestions that have really been of great help to improve our manuscript. Below, a brief point by point list of our corrections which are underlined in the text.

Reviewer 1

Reviewer's code: 03475059

Major comments

Remark 1. Was the sleeve sensor used for detecting the LES pressure? Since the LES was moved during swallow as well as respiration, the pull-through method cannot evaluate swallow-related LES relaxation.

Response 1: We did not use the sensor sleeve during this study. However, the equipment used and the manometry procedure met the American Gastroenterological Association recommendations.

In this study, at least 4 wet swallows were necessary to analyze the relaxation of LES.

Remark 2. There are several proposed causes of secondary achalasia such as Chagas disease. Is the Chagas disease in Algeria?

Response 2
No, Chagas disease does not exist in Algeria and it has never been described in.

Remark 3. The increase of prevalence of achalasia in recent studies may be based on the progress of evaluating esophageal motility. Is high resolution manometry used in your study? If the high resolution manometry is not used, the low prevalence of esophageal motility disorders may be due to old fashion of diagnostic methods.

Response 3

The high resolution manometry has not been used in this study. It was introduced in Algeria only in 2014. However, in this study the diagnosis of achalasia, was made on constellation of clinical, radiological, endoscopic and manometric features (conventional manometry).

Remark 4. What is the term "the mean delay diagnosis"? Does it mean the mean duration of diagnosing the achalasia?

Response 4

 Yes, the mean delay diagnosis means the duration of diagnosing achalasia.

Remark 5. Did you perform esophageal manometry in pediatric patients especially 3 month infant?   Were the normal values of manometric parameters same as adult patients?

 How did you assess symptoms in pediatric patients?

Response 5

 We perform esophageal manometry in pediatric patient older than 12 months.

Children aged less than 12 months have not benefited from manometry and diagnosis of achalasia was made on clinical, endoscopic and radiological data.

The pediatric manometry is performed exclusively in our department and all pediatric manometries of this study were performed by Prof. A. Tebaibia

- The normal values of manometric parameters are the same in both pediatric and adult patients.

- For infants, the parents answered the questions about the presence or absence, severity and frequency of the following symptoms: vomiting, regurgitation, weight loss, cough, respiratory infections and dysphagia was looked for in children aged over 5 years.

Minor comments

Remark 1. The CME should be spelled out at the first time in the abstract.

Response 1

CME (continuing medical education) was spelled out and added to the abstract

Remark 2. In the abstract, the sentence "Patients had dysphagia (99%), Regurgitation (83%), Chest pain (51%), heartburn 24.5% and weight loss (70%) " should be" Patients had dysphagia (99%), regurgitation (83%), chest pain (51%), heartburn 24.5% and weight loss (70%)".

Response 2

The correction was made in the text as follows

"Patients had dysphagia (99%), regurgitation (83%), chest pain (51%), heartburn 24.5% and weight loss (70%)".

Remark 3. In the statistical part, the fonts of the last 3 sentences were changed. The font should be modified.

Response 3

The correction was made in the text.

Remark 4. "Retro sternal, epigastric or inter scapulars pain" should be "Retro-sternal, epigastric or inter-scapulars pain".

Response 4

The correction was made in the text as follows:

"Retro-sternal, epigastric or inter-scapulars pain".

Remark 5. What is EB in the summary part?

Response 5

EB means esophageal body.

Reviewer 2

Reviewer's code: 03216660

1- The authors need to be congratulated for an excellent work performed over a period of 25 years describing very interesting findings on the epidemiology of achalasia in Algeria, in a very particular context related to the fact that there was a referral of all cases to a single center in Algiers.

Thank you very much.

Remark 2- The authors are proposing that Continuous Medical Education is responsible for the increase noted in the incidence of the disease. This is surely a possibility; however the document does not bring solid arguments to support this proposition. Maybe an addition on Figure 2 adding the moment of the main campaigns of education might be helpful?

Response 2

We added the moment of the main campaigns of CME in the figure 2.

Remark 3- The significance of CME should be defined earlier in the text.

Response 3

We have added the definition earlier in the text.

Remark 4- Is it possible that some patients were not diagnosed because of a limited access to the main institution in Algiers, e.g. because of the distance? This should be discussed.

Response 4

We believe that the incidence of achalasia is underestimated in Algeria, because of many factors, one of them is the limited access to the main institution in Algiers due to the distance and may

be to the economic and social conditions, especially for those coming from the south.

We have added it and discussed it in the text.

Remark 5- Figure 1 should be updated to give more information on the incidence of achalasia. It would be very interesting to see the overall incidence in time according to the province in which the patients are living, instead than a simple description of the Algeria provinces.

Response 5

Great idea. Figure 1 was updated.

As we had very low number of new cases per year for each province and to make statistical analysis easier, we gathered cases of different provinces in three regions.

We have added in the text the incidence and the number of cases for each region (north, high planes and south).

Remark 6- The statistical analysis reported is mainly descriptive. The authors would benefit from comparing some of their impressive results according to different factors, e.g. is there a significant trend in the change of incidence over time?

Is the time before diagnosis becoming shorter over time? Etc. Many of these questions could be easily answered with a more detailed inferential statistical analysis.

Response 6

- Yes, there is a highly significant trend in the change of incidence over time ($P < 0.001$). We added it in table 1.

- Yes, the time before diagnosis became shorter but there is no significant trend in the change of the duration. The mean delay diagnosis of achalasia from 1990 to 1997 was 75,78 months (IC 95 %:50,93 ; 100,63). From 1998 to 2005, it decreased to 54,68 months (45,39 ; 63,97) to reach a mean of 48,76 months (IC 95%: 43,22 ; 54,30) from 2006 to 2014.

Remark 7- Was there any patient investigated more than once? Are they included in the analysis?

Response 7

No patient was investigated more than once.

Remark 8- The authors have collected very well a large amount of information that could be highly valuable to define some details rarely reported on achalasia. One of them in my opinion is the time between the initial symptoms and the diagnosis. I think that the data available to the authors can be used to better define this finding.

Response 8

The data showed that there is a trend in the change of average age and mean symptoms duration before diagnosis. In fact, the time before diagnosis became shorter and the age younger but the difference was not statistically significant between the different periods.
We have added it in the text.

Remark 9- How consanguinity was defined in this study?

Response 9

It was defined as first or second cousins marriages.
We have added it in the text.

Remark 10- The document is well written overall.

Thank you very much.

Yours sincerely
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