OPEN PEER REVIEW

Revision (0)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Reply to requests and questions of reviewers

Reviewer 1

1 - key words have been selected based on MESH guidelines

2 - research type was indicated in page 2

3 - Primer referrence was introduced in table in page 14

4 - presence or absence of serotypes or screening based on multiplex PCR method , is qualitative and this study did not required sequencing

5 - the sampling time period was shown in page 4

6 - size of cpsA band in PCR method represented in pages 11 and 14

7 - statistical method was mentioned in page 7

8 - phenotypically prevalence of Pneumococci was indicated in page 5

9 - serotyping results briefly were added to abstract section in page 2

10 - The data of multiplex PCR for Pneumococcal serotype were indicated in article “Serotyping of *Streptococcus pneumoniae* isolated from Tehran by Multiplex PCR: Are serotypes of clinical and carrier isolates identical?” Sstudied by Seyed Fazlollah Mousavi,* Saman Nobari, Fatemeh Rahmati Ghezelgeh, Hamid Lyriai, Pantea Jalali, Fereshteh Shahcheraghi, and Mahvash Oskoui that printed in Iranian Journal of Microbiologyv.5(3); 2013 Sep. the frequency of Pneumococcal serotypes are the same in this study. This prevalence data was pointed out by referrence 37

11 – some comparisons were performed with other similar studies in discussion

12 - some update refferences were added

Reviewer 2

1 - structural failures were corrected and was shown in title

2 - routinly , since there is limitation for representation of pictures ,the hemolytic function of Pneumococci was not shown here.

3 - dear reviwer , we appreciate of your consideration about this study. Probabely something wrongfully has happened during the typing of requests. Please check the requests after question 2.

Reviewer 3

1 - a given part in introduction was removed in page 3

2 - the bobjective of this study pointed out in page 4

3 - we want to clear if there is any typical relation between native serotypes and neuraminidase as virulence factor or not. Also demonstrable relation between significant virulent serotypes and neuraminidases in Iran.

4 - relation between serotypes and neuraminidase genes is indicated in table 4 and

figure3

5 - some parts of discussion were removed from pages 7-9

OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://brieflands.com/briefland/knowledgebase/category/tree.html#opr.html

Archives of Pediatric Infectious Diseases
Article DOI: 10.5812/pedinfect.14100
Published in: Archives of Pediatric Infectious Diseases: 8(1); e14100

Peer Review Report for "Relationship Between Prevalence of Pneumococcal Serotypes and Their Neuraminidases in Carriers, Predictive Facts?"

Author(s): Fatemeh Norolahi, Seyed Davar Siadat, Mohammadali Malekan, Seyed Hamid Mousavi, Alireza Janani, Seyed Fazlollah Mousavi

Review Timeline:

Submit Date: 27 May 2017
Revised Date: 11 Dec 2019
Accepted Date: 23 Dec 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 23 Jun 2017

Dear AE,
Thanks for the revisions, comments for the authors:
1. Please describe the method of calculating the relation between Pneumococcal serotypes and prevalence of neuraminidases genes
2. Methods of statistical analyses should be described clearly
3. Discussion is still too exhaustive. It could be more focused.
Regards

REFEREE: Reviewer | **Revision** (0) 26 Jun 2017

Dear AE,
Comments for the authors:
- You should add discussion for abstract.
- CAT No. and the producer company names for used materials has not been mentioned.
- Sequencing method should perform to confirm the PCR accuracy (neuraminidase genes).

- What is the reference for primers in table3?
- Please add the NUMBER and percentage of pneumococcal strains that were positive in phenotypic assay.
- Are the results for serotyping in this study is the same as “Serotyping of Streptococcus pneumoniae isolated from Tehran by Multiplex PCR: Are serotypes of clinical and carrier isolates identical?.”? If not please delete reference number 37.
- English grammar and structures need revision.
- The conclusion is poorly written.
- More new references should be added from Archives of Pediatric Infectious Diseases journal.

Best regards.

REFEREE: Reviewer | **Revision** (0) 5 Jul 2017

Dear AE,

Relation between the prevalence of Pneumococcal serotypes and their neuraminidases in carriers, predictive facts?

Comments for the authors:

1. Please add the most common Pneumococcal serotypes in the world in the Introduction section.
2. Please add the type of study in the Materials and Methods section (line 56).
3. Please add preserving media that was used in this study in the methods section (line 60).
4. Please add the manufacturer of biochemical tests and media in the Materials and Methods section.
5. Please add the manufacturer of the Optochin disk test in the Materials and Methods section (line 68).
6. Please add the country of the DNA extraction kit in the Materials and Methods section (line 80).
7. Please compare results (including the number of isolates, nanA, nanB, nanC, and serotypes) according to the place of sampling (Tehran, Fars, Ardebil, Lorestan, Khorasan and Sistan Baluchistan) and add related data (in the table or figure).
8. Please add the most common serotypes in Iran in the discussion section.
9. Revise all numbers and percentages in the text, to ensure their accuracy.
10. Minor spacing problems exist between the words in some parts of the text.
11. Recheck the sequence of primers, to ensure their accuracy.
12. Please revise carefully all the references. Some of the references are not based on the journal guidelines.

Thanks

REFEREE: Associate Editor | **Revision** (0) 6 Jul 2017

Dear EIC,

The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.

Kind regards,

REFEREE: EIC | **Revision (0)** 12 Jul 2017

Dear Author,

The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Here are responses and answers to minor revision that reviewers demand to consider for article titled " Relation between prevalence of Pneumococcal serotypes and their neuraminidases in carriers , predictive facts? "

All the corrections and revisions blue hihlighted

Reviewer 1:

1. *Please add the most common Pneumococcal serotypes in world in Introduction section.*

These serotypes were remark in lines 23-25

2. *Please add the type of study in in Materials and Methods section (line 56)*

In line 59 , study type in the beginning of paragraph was added

3. *Please add preserving media that used in this study in methods section (line 60)*

In lines 64-65 the presevatory medium was added

4. *Please add the manufacturer of biochemical tests and media in Materials and Methods section.*

In lines 64, 65 ,69,74 , 75 , 79, 101 the producers and manufacturers of materials were mentioned

5. Please add the manufacturer of Optochin disk test in Materials and Methods section (line 68)

The Optochin disk producer was mentioned in lines 74,75, 79

6. Please add the country of DNA extraction kit in Materials and Methods section (line 80)

Producer country of DNA extraction kit was noticed in lines 86, 87

7. Please compare results (including number of isolates, nanA, nanB, nanC, and serotypes) according to place of sampling (Tehran, Fars, Ardebil, Lorestan, Khorasan and Sistan Baluchistan) and add related data (in the table or figure).

In lines 213 – 215 , briefly described

8. Please add the most common serotypes in Iran in discussion section.

the most common serotypes in Iran in discussion section based on refernce 37 , were indicated in lines 157-160

9. Revise all numbers and percents in the text, to ensure their accuracy

All numbers and percents in the text were revised and there was no mistake between them

10. Minor spacing problems exist between the words in some parts of the text

The spacing problems were corrected .

11. Recheck the sequence of primers, to ensure their accuracy

sequence of primers were rechecked and there were no mistakes between them

12. Please revise carefully all the references. Some of the references are not based on the journal guidelines.

all references were rechecked and some failures were corrected

Reviewer 2:

1 - You should add discussion for abstract.

In lines 16 – 18 partially discussion was added

2 - CAT No. and the producer company names for used materials has not been mentioned.

In lines 64, 65 ,69,74 , 75 , 79, 101 the producers and manufacturers of materials were mentioned

3 - Sequencing method should perform to confirm the PCR accuracy (neuraminidase genes).

In lines 118 – 119 , it was briefly described

4 - What is the reference for primers in table3?

The primer reference for primers was mentioned in table 3 in line 225

5 - Please add the NUMBER and percentage of pneumococcal strains that were positive in phenotypic assay

It was mentioned in line 124

6 - Are the results for serotyping in this study is the same as "Serotyping of Streptococcus pneumoniae isolated from Tehran by Multiplex PCR: Are serotypes of clinical and carrier isolates identical?."? If not please delete reference number 37.

They are comparable

7 - English grammar and structures need revision.

As far as it was possible , we improved the English fluency

8 - The conclusion is poorly written.

Conclusion was partially more descreibed in lines 213 – 218

9 - More new references should be added from Archives of Pediatric Infectious Diseases journal.

referrence number 40 was added and referred on article text in line 143

Reviewer 3:

1. Please describe the method of calculating the relation between Pneumococcal serotypes and prevalence of neuraminidases genes

The statistical methods for calculating the relation between Pneumococcal serotypes and prevalence of neuraminidases genes and analysis was described partially in lines 120 – 121

2. Methods of statistical analyses should be described clearly

The statistical methods for calculating the relation between Pneumococcal serotypes and prevalence of neuraminidases genes and analysis was described partially in lines 120 – 121

3. Discussion is still too exhaustive. It could be more focused.

The statistical methods for calculating the relation between Pneumococcal serotypes and prevalence of neuraminidases genes and analysis was described partially in lines 120 – 121

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) — 5 Apr 2018

Dear AE,
1. I could not find the methods and the results of calculating the relation between Pneumococcal serotypes and prevalence of neuraminidases genes.
2. The main axis of the discussion is not clear
Regards

REFEREE: Reviewer | **Revision** (1) — 6 Apr 2018

Dear AE,
Comments for the authors:
- Name of genes should be in italic form.
- Sequencing analysis should be added to the manuscript.
- Please add some new references with Endnote.
- English grammar and structures need revision.
Best regards.

REFEREE: Reviewer | **Revision** (1) — 10 Apr 2018

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Associate Editor | **Revision** (1) — 10 Apr 2018

Dear EIC,
The manuscript needs MINOR REVISION.
Best regards.

REFEREE: EIC | **Revision** (1) — 10 Apr 2018

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.

Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Reply to reviewers

Reviewer 1 :

1 - *I could not find the methods and the results of calculating the relation between Pneumococcal serotypes and prevalence of neuraminidases genes.*

Reply : the methods of calculating was indicated in lines 121 – 122 and their results were shown in table 4

2 - *The main axis of the discussion is not clear*

Reply : the main axis of discussion clearly was indicated in lines 170 – 172

Reviewer 3 :

1 - *Name of genes should be in italic form*

Reply : the names of genes were corrected as italic form

2 - Sequencing analysis should be added to the manuscript.

Reply : sequencing was shown in lines 118 – 120

3 - Please add some new references with Endnote

Reply : the new referrences 37 – 40 , were added

4 – English grammar and structures need revision

Reply : the English structures were as possible corrected.

Thank you for your attention

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (2) 30 Oct 2018

Dear EIC,
The manuscript needs major revision.
Best regards.

REFEREE: Reviewer | **Revision** (2) 31 Oct 2018

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Reviewer | **Revision** (2) 4 Nov 2018

Dear AE,
Thanks for the manuscript
1. The results in table 4 don't indicate the relationship between Pneumococcal serotypes and the prevalence of neuraminidases genes
2. Repeating the main goal of the study in discussion does not mean that the main goal of the discussion is clear. The relevance of lines 137-154 to the results of the study is not clear.
Regards

REFEREE: EIC | **Revision** (2) 12 Nov 2018

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (3)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Dear reviewer 1:

Thank you for your comments. Two points you indicated, corrected as following:

1 - As indicated in highlighted lines 133 – 143, some additional information were annexed to results and these data can clarify better the relation between serotypes and presence or absence of *nan* genes.

2 - The highlighted lines 164 – 173 were added to discussion section, so this description makes a better relation between main goals and conclusion of study.

With the best regards

OPEN PEER REVIEW

Revision (3)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (3) 23 Jan 2019

Dear EIC,
This study focuses on the relation between Pneumococcal stereotypes and the prevalence of neuraminidases genes… but there is no statistical analysis to estimate this correlation.
Best regards.

REFEREE: Associate Editor | **Revision** (3) 7 Feb 2019

Dear EIC
The reviewer(s) have recommended publication, but also suggest some major revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision** (3) 9 Feb 2019

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

OPEN PEER REVIEW

Revision (4)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Dear Editor in Chief,

Thank you so much for getting back to us with the reviewers' comments. We appreciate your reviewers' time, and believe the quality of our manuscript have improved substantially after addressing the reviewers' comments.

Reviewer #1:

Dear author:

This study focuses on the relation between Pneumococcal serotypes and the prevalence of neuraminidases genes..... but there is no statistical analysis to estimate this correlation.

Best regards.

Authors' response: Thanks for your time and valuable comment. We would like to acknowledge that due to the existing knowledge gap in Iran, the aim of this study was to evaluate the extend of pneumococcus carriage in children of Iran as well as the distribution of pneumococcus serotypes and neuraminidase genes in these carriers. In the new version of the manuscript, we revised our objectives in order to make it clearer(Introduction section, last paragraph). We also further elaborated on the statistical methods used in our study (Methods section).

Associate Editor #2:

1 – Number of samples gathered from each province and number of positives should be provided.

Authors response: Thanks for your point. We added this data into the revised manuscript (Please see the new Table 3 and 4).

2 – Statistical methods are completely uninformative.

Authors response: Details on statistical methods are now provided in the Methods section (Methods section).

3 – Add 95% CI calculation method.

Authors response:WilsonScore interval method was used to estimate 95% Cis. We mentioned our estimation method in the text and footnote of the revised Table 3 and 4.

4 – Figure 3 should be deleted; information already provided in the text

Authors response:We omitted Figure 3.

5 – Please report 95% CI for main outcomes for example 100% nanA positive (with Wilson Score interval method 100% with n=92 gives 95% CI. 95.99-100.00)

Authors response:Thanks for your comment. We calculated 95% CI for the main outcomes using the Wilson Score interval method.

6 – In “line 130”, percentages 97% and 62% should be rechecked. According to the table-4, there are 79 and 57 nanB and nanC positives, respectively, that indicates 85.8% nanB and 35.3% for nanC.

Authors response: Thanks for raising this point. You are right, there were 79 nanB and 57 nanC positives which gives a frequency of 85.9% and 62.0%, respectively. We corrected these numbers in the text.

~~79 (85.9)~~	~~77.3, 91.6~~	~~57 (62.0)~~	~~51.8, 71.2~~

7 – The concept of “relation” in this study is different from “correlation” or any other statistical relationships; and there is no statistical tests output in the result. By reporting frequency of nan genes in study sample, I can / may name these frequencies as “percent agreement”. So, please change “relation” to some other meaningful terms.

Authors response:Thank you for your comment. You are right. The aim of this study was to evaluate the extent of pneumococcus carriage in children of Iran, as well as the distribution of pneumococcus serotypes and neuraminidase genes among these carriers. So, we did not aim to test for correlations. In the new version of the manuscript, we revised our objectives and wordings in this regard. We also further elaborated on the statistical methods used in our study (Methods section).

8 – Also change “prevalence” to “frequency”.

Authors response: we changed the word “prevalence” to “frequency” in the text and in the tables and figures.

OPEN PEER REVIEW

Revision (4)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision (4)** 13 Jun 2019

Dear AE,
This is a study on “Pneumococcal serotypes and their neuraminidases in pharyngeal carriers”. Its primary aim is to determine incidence of different candidate serotypes and cpsA and NA (A, B and C) in six provinces in Iran. Its second aim is to investigate correlation between serotypes and NA distribution.
- From the point of view of the language, English is quite poor and should be revised. It is difficult to understood in many parts.
For example: "Since 202 the serotypes 4 and 12F frequently have been indicated in invasive infections, this study searched for nanC gene" is difficult to understand.
- Writing style likes “Persian style” in some parts. For example, "… Multiplex PCR and if we refer to their study, we can see that frequency of Pneumococci serotypes in our country show some more percentage than this study."
- Scientific writing is not considered in some part, for example: "typical studies" is not correct.
- Authors should obtain valid certification before next submission.
- Please seek “English edit” by “Kowsar English Editing Services” at: [https://kowsarpub.com/en/index.php/services/for-authors/163-author-services/242-english-editing-services-by-authors].
- Paper suffers from numerous repetitions in discussion part. Discussion part should be started with overall finding and continued by separated paragraphs ordered similar to the result part, and finally terminated by the paragraph about advantages and limitation of the study.
- In addition to necessary English copy-editing, my main concern is with the results and discussion.
- It is recommended that all investigated serotypes (20) divide to invasive and non-invasive types and NA phenotype be divided into A/B (non-C) and C phenotype. Then these categorical variables analyzed with proper statistical test (need to consult with your statistical advisor)
- I think that for better understanding, discussion should be categorized to three parts. First, the overall incidence of serotypes and discussion about its difference between six provinces. Second, overall incidence of cpsA and NA. Finally, correlation between serotype and cpsA and NA.
- It should be noted that, discussion part should be started with overall findings and then ordered based on presented results in the result section. Limitations and advantages should

be discussed before final conclusion in the last part of discussion part.
Other shortcomings:
Abstract:
- “non-serotypes” or “none” have been used several times in text (abstract and …) and tables (Table 3 and 4), simply you can use “non-typable” if you have some isolates that could not be recognized by designed primers.
- Study results should not be generalized. Rewrite this statement: "Our results showed that about a quarter of children were Pneumococcus carrier".
- In “Keywords”, Add "pharyngeal carrier". Replace this keyword "serotype", with "serotyping". Add “colonization”.
- Whenever "Pneumococcus carriage" is used in the manuscript, colonization site should be determined. For example, nasopharyngeal or pharyngeal.
Introduction
- Clinical importance of nasopharyngeal colonization should be mentioned in the introduction not in discussion.
- Citation style is not correct: "(1, 2, 3, 4)", (1-4) is correct.
- Remove this part: "The structural analysis of Pneumococcal neuraminidases indicates that fifty percent of NanB and NanC sequences are similar but 25% of their sequences are similar with NanA (6, 7)".
- Rewrite this part: "This study aimed to investigate the extent of Pneumococcus carriage among Iranian children", "among Iranian children" should be replace with proper words such "in six provinces in Iran".
- This part contain repetition: "Susceptibility of bacteria to Optochin disks 85 (Mast diagnostics Cat.no. D42) ...", remove "(Mast diagnostics Cat.no. D42)". It is declared previously in line 80-81.
Discussion
- In this phrase: "There are two types of vaccines that are used to prevention of Pneumococcal infections.", vaccine types should be defined.
- This statement may be changed after new analysis "it could be concluded that there is no meaningful relation between Pneumococcal serotypes".
- Reconsider this statement: “Sixteen serotypes of Pneumococcus were studied in our …”. 16 or 20? (see table 1)
- This is not true conclusion: "High frequency of nanA and nanB in our study indicates that these genes are required for Pneumococcal colonization and pathogenesis", this study is not designed to address this goal.
Thanks

REFEREE: Reviewer | **Revision (4)** 18 Jun 2019

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Associate Editor | **Revision (4)** 21 Jun 2019

Dear EIC,

The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

REFEREE: Associate Editor | **Revision** (4) 1 Jul 2019

Dear EIC,
The manuscript needs minor revision.
Best regards.

REFEREE: EIC | **Revision** (4) 9 Jul 2019

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (5)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Dear Editor in Chief,

Thank you so much for getting back to us with the reviewers' comments. We appreciate your reviewers' time, and believe the quality of our manuscript have improved substantially after addressing the reviewers' comments.

Reviewer 2:

Thanks for your time and valuable comment. We would like to acknowledge we sent our manuscript to Kowsar English edition services for English edition and we obtained valid certification for English edition.

Other your comments were revised as follows:

- "Non-serotypes" or "none" terms were uniformly turned into non-typable and "nasopharyngeal" or "pharyngeal" uniformly turned into nasopharyngeal.
- In keywords, "colonization" and "pharyngeal carrier" were added and "serotype" replaced with "serotyping"
- Clinical importance of nasopharyngeal colonization mentioned in introduction.
- Citation style as (1,2,3,4) uniformly was corrected throughout the manuscript as (1-4).
- Carriage among Iranian children replaced with among six provinces of Iran
- Repetition of optochin susceptibility was corrected and rewrote it continuously.
- Repetition of (Mast diagnostic Cat.no. D42) was corrected.
- As far as possible , we corrected discussion based on your comments.
- There is no incidience rate for cpsA gene and correlation between cpsA, serotypes and NA because this gene is not epidemiological marker for Streptococcus pneumoniae and uniformly exists among Pneumococcal serotypes. cpsA gene only are used for molecular detection of Pneumococci in clinical samples.
- On the other hand, rest of your comments automaticaly were corrected after English revision by Kowsar English edition service.

Thank you for your comments.

OPEN PEER REVIEW

Revision (5)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Ali Amanati: Associate Editor | **Revision** (5) 9 Nov 2019

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision** (5) 12 Nov 2019

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (6)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Dear reviewer

Thank you again for your points and time you spent on this manuscript

1 –Discussion part automatically starts with some overall findings

2 - Two first paragraphs from “Discussion part” (from “About 60% of bacterial pneumonia” to “combat pneumococcal infections.”. were removed

3 – Some suggestions about this study were added in lines 187 – 193

4 - conclusion part was provided with distinct title after conclusion in line 159

5 – The part: “Hence, serotypes 3 and 14 can be the main causes of HUS and IPD in carriers.” Was removed.

6 – The part: “The results showed that these serotypes could also be the main causes of invasive infections including hemolytic uremic syndrome (HUS) and meningitis in carriers.” Was removed.

7 – The part: “High frequency of nanA and nanB in the current study indicated that these genes are required for pneumococcal colonization and pathogenesis; also, nanC gene is necessary for pneumococcal invasion to body organs such as central nervous system and development of meningitis and HUS following necrotizing pneumonia. It can be concluded that a complex of these genes could be a promising candidate for designing and producing effective new vaccines against pneumococcal diseases in Iran. Nevertheless, confirmatory studies are required to obtain more conclusive results” was removed.

Thanks

OPEN PEER REVIEW

Revision (6)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision** (6) 7 Dec 2019

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (7)

Reply to Reviewers

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You can read the authors' responses to the reviewers' comments in the next page.

Dear Editor in Chief,

Thank you so much for getting back to us with the reviewer's comment. We appreciate your reviewer’s time, and believe the quality of our manuscript have improved substantially after addressing the reviewers’ comments.

Dear Reviewer

Thanks for your time and valuable comment. We would like to acknowledge we reduced conclusion part into ten lines and one paragraph.

Thank you for your comment.

OPEN PEER REVIEW

Revision (7)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision** (7) 23 Dec 2019

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.