Author’s response to reviews

Title: The association between Interleukin-28B gene polymorphisms as a potential biomarker and the risk of Chronic Periodontitis in an Iranian population

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Title: The association between Interleukin-28B gene polymorphisms as a potential biomarker and the risk of Chronic Periodontitis in an Iranian population

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Dear Editor in-chief

Thanks for the kind comments regarding our manuscript. Reviewer’s comments were read carefully, all questions were answered, and requested modifications were done according to reviewers’ points of view. Some sentences were revised in the main-text and new changes marked by red color. We hope that this revision of manuscript could qualify it to be published in the” Head & Face Medicine”.

Yours’ sincerely

Bita Moudi
Reviewer comments:

Reviewer 1:

I congratulate author for a good manuscript. Study looks novel/original and a good study design.

I feel few important points should be revised/ added.

1) method of calculation of sample size

2) how no of cases and control are decided

This study was a case-control study. We had a chance to do the project and collect the samples from September 2015 until March 2016. During this period of time we investigated all individuals referred to the Periodontology Department, Dentistry Clinic of Zahedan University of Medical Sciences (ZUMS), as the only referral center. These persons, considering inclusion and exclusion criteria, all people who had clear signs of the chronic periodontitis were selected as cases (n=210) and people who were perfectly healthy and referred for cosmetic treatments, were selected as controls (n=100). Matching between groups regarding age, ethnicity, and gender were done and finally this number of cases and controls were achieved.

3) elaboration of role of IL-28B in pathology of Chronic Periodontitis.

Interleukin 28B (interferon-λ 3) is a protein that in humans is encoded by the IL28B gene and has recently been renamed IFNL3 as its official gene symbol. This gene encodes a cytokine distantly related to type I interferons and the IL-10 family. This gene, interleukin 28A (IL28A), and interleukin 29 (IL29) are three closely related cytokine genes that form a cytokine gene cluster on a chromosomal region mapped to 19q13. Expression of the cytokines encoded by the three genes can be induced by chronic infection such as chronic periodontitis. All three cytokines have been shown to interact with a heterodimeric class II cytokine receptor that consists of interleukin 10 receptor, beta (IL10RB) and interleukin 28 receptor, alpha (IL28RA). The selected SNPs are located in regulating regions of IL28B gene which can control the expression of the gene. On the other hand, gene variations can change the biological function of gene. There is a little information about the relationship of these two polymorphisms and regulation of expression of the IL28B gene. Therefore, for the first time, in this study, we aimed to investigate the relationship between rs8099917 and rs12979860 polymorphisms and CP. Also Previously, we have studied the relationship between polymorphisms of inflammatory and proinflammatory genes and chronic periodontitis. In this study, given the pervasiveness of chronic periodontitis in Iran and the importance of IL-28 in the pathogenesis of inflammation, we decided to examine the impact of these cytokine SNPs in susceptibility to CP . The aim of this paper was to investigate the association between two single nucleotide polymorphisms, rs8099917 and rs12979860, and
CP. Further clarification about the role of IL-28B in pathology of Chronic Periodontitis had been provided in the paper.

Reviewer 2:
Language review - very good
NO COMMENT.

Reviewer 3:
In the Introduction the authors should review the references presented. In fact they referenced some recent work but there are more recent and international one about genetics and chronic periodontitis. To make the work more independent and scientifically correct, they must be more international in the reference selection as well as in the cited journals.

The state of the art needs to be improved!!

SOME NEW REFERENCES WAS ADDED (4,11-17,25-31).

In the Study subjects the sentences "Study population was selected from outpatient department of the Periodontology, Dentistry Clinic of Zahedan University of Medical Sciences, Zahedan, Iran, as previously described [17]. In summary, a total of 210 patients with CP and 100 healthy controls were recruited." need to be reformulated.

The authors have to explain what is "outpatient" as well as the sample selection - Why were 210 patients and not 100?, Why they choose the control group with 100 patients?

Revisions were done in material and method part. In response to the reviewer 1 we respond to this question.

The authors should explain the sentence "All volunteers were nonsmokers, had at least 20 teeth and were Iranian ethnicities from the South East of Iran". Iranian ethnicities are not clear...

There are three main ethnicities in South-East of Iran; Baluch, Sistani and others. Case and control groups were matched regard to the ethnicity, gender and age. These explanations were added to the text.

The English has to be improved!!

IT WAS DONE.