Re: **Hospitalizations due to Angioedema Without Urticaria in a Portuguese Center: 5-years Retrospective Study (#11893).**

Dear Editor,

We would like to thank the reviewers for this second analysis this manuscript. We have answered the few comments and suggestions that were made by the reviewers.

Our response follows (the reviewer’s comments are in italics) and all the changes in the manuscript body are highlighted in red.

**Revisor A:**

*Nova revisão*

*Desde já agradeço aos autores a revisão dos pontos assinalados, mas umas das principais anotações realizadas e passo a citar:*

*“ como o objetivo do estudo é avaliar a prevalência e a etiologia dos internamentos por angioedema sem urticária, não me parece pertinente incluir os doentes com diagnóstico de angioedema hereditário (não estando em fase de agudização)”não foi contemplada. No meu ponto de vista, angioedema como sinal ou sintoma que motiva ou complica um internamento, não é a mesma coisa que um doente ter défice de c1 inibidos e ser internado para fazer a sua reposição para evitar angioedema. Portanto, continuo da opinião de que o ponto C não parece ser um bom critério de inclusão.*

**Resposta:**

Muito obrigada pela nova leitura do manuscrito.

O texto do manuscrito foi revisto e alterado, tendo sido excluídos os internamentos contemplados no grupo C. As alterações encontram-se indicadas a vermelho no texto do manuscrito. A análise estatística foi ajustada tendo em conta a nova amostra considerada. Foi usada uma versão mais recente do software SPSS para esta nova análise.

As tabelas e imagem do artigo também foram alteradas, tendo em conta as sugestões do revisor A.

***Revisor B:*** *I have just one more comment to address to the authors, and it is related to
the alternative test of the asymptotic chi-square test, Fisher's exact test.
This is not a possibility in this case because it can only be used when comparing 2 groups with respect to a binary variable. Hence I asked whether it would be the exact chi-square test or the Monte Carlo simulations method. One of these will have to be used. Thank you.*

**Resposta:**

We are very thankful for your careful reading of the manuscript and also for your statistical suggestion.

As indicated by reviewer A, we have excluded some patients from our analysis. For this reason, in this second version of the manuscript, we were only included 169 patients (the 32 patients that were hospitalized for hereditary angioedema prophylaxis treatment were not considered).

Besides this, we have also used a more updated version of SPSS software (SPSS 24®) for the statistical analysis.

Considering this changes and your suggestions, the “statistical analysis” section of the manuscript’s methods was re-written (all changes are in red).

We have also reviewed all the statistical analysis preformed in our revision after excluding the 32 patients from our sample. For this new analysis, we used the Monte Carlo estimate of Fisher’s exact test (the references that support our choice is included in <http://www.sussex.ac.uk/its/pdfs/SPSS_Exact_Tests_21.pdf> ), except for comparisons between the means where we used the Kruskal-Wallis test.

Answering to your question regarding the Fisher exact test, SPSS provide the Fisher-Freeman-Halton Exact Test for contingency tables that are larger than 2x2 (<https://www-01.ibm.com/support/docview.wss?uid=swg21479647>). Therefore, using SPSS 24 version, we know that result labeled as Fisher's Exact test in the output is in fact the Fisher-Freeman-Halton Test.

All changes are indicated in red in the manuscript. The tables and the figure of the manuscript have also been updated according to these new reviewers’ suggestions.

Yours sincerely