Reviewer’s report

Title: Role of C-reactive protein as a biomarker for prediction of the severity of pulmonary exacerbations in patients with cystic fibrosis.

Version: 2 Date: 7 July 2014

Reviewer: Kelly Moffitt

Reviewer’s report:

This research article seeks to investigate whether CRP levels could be used to predict the severity of pulmonary exacerbations in patients with Cystic Fibrosis and concludes that there is no relationship between CRP levels and severity of exacerbation.

The article is well written and both the title and abstract convey what has been found in their study. The focus of whether CRP levels are associated with the severity of pulmonary exacerbations is addressed throughout the paper. The authors make mention of other work within this area upon which they are building and also results from similar studies. The methods are appropriate and well described. The development of a robust severity index for pulmonary exacerbations would be a very useful tool in the management of CF, particularly as it focusses on lung function and complications.

There are two clear limitations to the study –
(i) Limited Cohort – There are only 27 patients with ~ 2 hospitalisations each which will produce limited data and;
(ii) CRP is a systemic non-specific biomarker therefore not ideal for the study of pulmonary exacerbations

These limitations have been acknowledged and clearly referred to throughout the article.

Major Compulsory Revisions:

I have some issues regarding the reporting of the investigations that I would recommend as needing to be addressed:

1. The authors report an association between CRP levels and P. aeruginosa and aspergillosis. However, they do not report their findings regarding other bacteria which were colonising the patients, in particular, the 66.7% who were colonised with S. aureus. The authors quote Watkin et al as finding lower CRP in patients with S. aureus – did the authors of this study find the same lower levels?

2. There is a poor representation of data in the results section and better use could be made of results – basically findings are summarised into one table. There should be other graphical representations to compare results before and after exacerbation in chart form and also correlation graphs between several of the parameters.
3. Correlations should be made between CRP and other inflammatory biomarkers such as IL-8 and HNE. The authors present values for IgG, IgA and IgM – were these total titre values – if so, then these are non-specific or where they against P. aeruginosa antigens for example?

Recommendations for Improvement:
1. The discussion section should contain more specific information with regards to correlation of CRP to well documented specific pulmonary biomarkers such as IL-8 and NE. There is little mention to the inflammatory biomarker values reported in table 2. Was there any correlation with the antibody titres and other inflammatory markers with the severity index?
2. Neutrophil Elastase mentioned in the discussion is an important biomarker in detecting and monitoring pulmonary exacerbations. This biomarker has been found to correlate with CRP therefore, was this measured in the study? Of particular note, this biomarker may be more relevant to the severity index rather than CRP.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.