RESPONSE TO REVIEWERS

Thank you for giving us the opportunity to submit a revised draft of the manuscript. We are most grateful for the time the editors and reviewers spent on providing suggestions on how to improve our paper. In our revision, we have tried to address all the concerns raised by the editor and the reviewers.

REVIEWER 1

Specific Comments to Authors: This study highlights the role of cost-effective, readily available biomarkers fibrinogen and albumin in predicting angiographic severity and clinical outcomes in patients with acute coronary syndrome. Fibrinogen to albumin ratio independently predicted outcomes with greater accuracy compared to fibrinogen or albumin alone. However, there are some issues that need further clarification to improve the quality of the article.

1. This paper identifies coronary artery trunk occlusion in patients with myocardial infarction by the detection of biomarkers and does not assess the severity of coronary lesions seen by CAG, which may also be significant in this regard.

Response: A very valid point made by the reviewer and we thank the reviewer for bringing it to our notice. We have accordingly analysed the available coronary angiograms (CAG) and calculated the SYNTAX score to determine the coronary lesion severity. Out of the 152 patients who underwent CAG, 132 could be retrieved and reanalysed. The Fibrinogen to albumin ratio (FAR) increased significantly with increasing SYNTAX score. Accordingly the FAR values in low SYNTAX (<22), intermediate SYNTAX (22-33) and high SYNTAX (>33)

were 15.8 ±2.9, 18.4 ±3.3 and 22.9 ±4.2 respectively ($p<0.001$). The same has been mentioned in the results section.

2. The time from onset to consultation was not given for the included ACS patients. In addition, it is desirable to have uniform standards to support the proper nouns involved in the text, such as the diagnosis of ACS.

Response: Another important suggestion by the reviewer. As suggested we have calculated the time of presentation to hospital in relation to the onset of chest pain. The mean duration of presentation to our hospital after chest pain was 12.8 ±9.9 hours. This is much higher compared to other international data as our centre is a large tertiary care centre where most of the patients are referred from smaller centres and in general are high-risk patients with large proportions having a complicated course. The presentation timing was not different amongst the patients with TIMI- ≤ 1 flow or TIMI-≥ 2 flow as highted in table 2 (13.4 ±11.2 vs 12.3 ± 8.8 hours; p=0.24).

3. A detailed description of the fibrinogen and albumin assays is desirable. In addition, fibrinogen results may be influenced by pre-sampling treatment and whether 24 hours after admission may affect the test results.

Response: As suggested additional description of the fibrinogen and albumin assays have been added. Venous blood samples were taken within 24 hours of admission and prior to angiography and prior to thrombolysis in case of STEMI for all the recruited patients. No blood samples of fibrinogen and albumin were withdrawn beyond 24 hours of admission or after thrombolysis or percutaneous transluminal coronary angioplasty.

4. Inflammatory markers were addressed several times in the discussion and no other inflammatory markers were addressed in the statistical tables.

Response: An excellent observation by the reviewer. The prime inflammatory markers assessed in our study were Fibrinogen and albumin. The only other inflammatory marker analysed was C-reactive protein (CRP). No other inflammatory markers were assessed and we accept that this is a limitation in our study. The reason for the same is because ours is a tertiary care centre predominantly catering to the weaker economic sections where curtailing the cost of treatment is a priority. Hence, we usually restrict investigation to affordable and cost-effective biomarkers that can be relied upon during patient management. We have included data on CRP in the results section and table 2 as advised by the reviewer**.**

5. The conclusion section lists some new biomarkers without specifying their specific role in the management of patients with ACS.

Response: We would like to bring to the notice of the reviewer that we have not added the role of any new biomarker in the conclusion section and our sole focus in this study has been the applicability of old, cost-effective and easily available biomarkers to effectively triage and identify this high-risk subgroup amongst ACS patients.

6. The COVID-19 has reduced the number of emergency heart attack visits and affected their prognosis, and these patients also cannot be tested for these biomarkers and remain ineffective in identifying spontaneous recanalization of the responsible vessels.

Response: We completely agree with the reviewers comments on the applicability of these tests in the times of a COVID-19 pandemic. However, we still believe that these easily available biomarkers with rapid turn-around might come in handy to triage patients with ACS

during COVID-19 pandemic where appropriate resource allocation remains the top most priority.

REVIEWER 2

This study has an interesting topic. Authors explored the role of cost-effective, readily available biomarkers fibrinogen and albumin in predicting angiographic severity and clinical outcomes in patients with acute coronary syndrome. The manuscript has delivered important clinical message and should be of great interest to the readers. However, several factors limit the publication of the paper in its current form.

Response: We thank the reviewer for taking out time and reviewing our paper with great dedication. We are thankful for the kind words of appreciation and welcome all the concerns of the reviewers.

1. The sample size of this study is too small. It's hard to powerfully support their results.

Response: An important observation by the reviewer with which we completely agree. We accept the criticism and have already stated the same in the limitation section. We hope this would pave way for further large-scale studies to affirm role of fibrinogen and FAR in predicting outcomes amongst ACS patients.

2. Authors should compare fibrinogen, albumin and fibrinogen albumin ratio with other easily available inflammatory biomarkers, such as CRP, WBC, ESR, NAP score, and so on,

to confirm the advantages of fibrinogen and albumin in predicting angiographic severity and clinical outcomes in ACS patients.

Response: We thank the reviewer to bring this very important aspect to our notice which will help improve the quality of our paper further. We would like to bring to the notice of the reviewer that we have not evaluated ESR and NAP scores in our population. WBC was evaluated but it did not have any correlation with mortality or angiographic severity as already shown in table 2. CRP levels did correlate with mortality and was significantly higher in non-survivors (56.4 ± 24.3 vs 35.2 ± 18.4, $P=0.04$). However no correlation of CRP was seen with angiographic severity or TIMI flow (47.2 ± 34.3 vs 39.7 ± 28.4, $p=0.16$). The same has been added in text and in table 2. FAR correlated with both mortality and angiographic severity and hence was superior to these biomarkers in our study.

3. NSTEMI and UA would have different incidence rate of totally occlusive lesions in NSTEACS patients. Subgroup analysis should be performed.

Response: As suggested by the reviewer, the same has been included in text in the results section.

Once again we sincerely thank the reviewers and the editor for their invaluable comments and welcome further suggestions if any.