

REVIEWER'S REPORT

Manuscript No.: JNHM-167

Title: *The biochemical features, physiological aspects, and clinical applications of serum amyloid A: a review.*

Recommendation:

Accept as it is

Accept after minor revision.....

Accept after major revision ☒

Do not accept (*Reasons below*)

Rating	Excel.	Good	Fair	Poor
Originality			☒	
Techn. Quality			☒	
Clarity		☒		
Significance		☒		

Reviewer's Name: Mr Sahil Srivastava

Detailed Reviewer's Report

The manuscript provides a broad review of serum amyloid A (SAA), covering its biochemical characteristics, physiological functions, inflammatory mechanisms, and potential clinical applications. The topic is relevant and clinically significant, and the manuscript includes a relatively recent reference base. The organization into biochemical, physiological, and clinical sections is appropriate.

However, major revision is required before publication. Several scientific statements are overly broad, some claims appear stronger than the supporting evidence, and there are terminology, grammar, citation, and factual consistency issues that need correction.

Major Comments

1. Clarify the distinction between SAA as a biomarker and SAA as a pathogenic mediator. The manuscript alternates between describing SAA as a biomarker and as a causal mediator. These roles should be clearly differentiated, particularly when discussing cardiovascular disease, cancer, infection, and metabolic disorders.
2. Correct factual/structural inconsistencies. The statement that SAA1/SAA2 are located on chromosome 11p15 but that SAA4 and the other genes are located close to them on chromosome 1 is internally inconsistent and should be corrected.
3. Avoid unsupported superiority claims. Statements such as SAA being “superior” to CRP or procalcitonin, particularly for neonatal sepsis and pediatric infection, require direct supporting studies. The manuscript should distinguish between potential utility, association, diagnostic accuracy, and demonstrated clinical superiority.

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4. Strengthen the evidence-based comparison with CRP. - The manuscript repeatedly states that SAA is more sensitive than CRP. This should be presented in a disease- and context-specific manner rather than as a generalized conclusion. Appropriate comparative studies or meta-analyses should be cited.
5. Review citation accuracy.- Some references do not appear to directly support the specific statements for which they are cited. Each major clinical claim should be checked against the original reference, particularly claims concerning neonatal sepsis, cancer prognosis, cardiovascular risk, and treatment monitoring.
6. Improve the clinical application section. -The clinical section covers many diseases but largely describes potential applications without adequately discussing limitations, diagnostic cut-offs, assay variability, sensitivity/specificity, reference ranges, and current clinical availability. The authors themselves acknowledge assay standardization as an unresolved issue.
7. Discuss limitations of SAA measurement more explicitly. -A dedicated subsection addressing assay standardization, biological variability, isoform differences, reference intervals, and lack of universally accepted clinical thresholds would substantially improve the review.
8. Avoid excessive repetition. -Concepts such as acute-phase response, HDL interaction, inflammation, and AA amyloidosis are repeated across the Introduction, Biochemical Features, Physiological Aspects, and Clinical Importance sections. These can be consolidated to improve readability.

Minor Comments

1. The sentence in the Introduction stating “The central importance of CRP...” appears inappropriate in a manuscript focused on SAA and should be checked for a possible typographical or conceptual error.
2. Several sentences require grammatical revision, for example:
 - “SAA are highly conserved...” should be grammatically corrected.
 - “The SAA is...” is repeatedly used where “SAA is...” would be more appropriate.
 - Several sentences are excessively long and should be divided.
3. There are multiple spacing and formatting problems, including terms such as “clinicalapplications,” “inflammatoryconditions,” and other merged words.
4. The manuscript should consistently use either serum amyloid A (SAA) or SAA after the first definition.
5. The term “systemic amyloid A” in the abstract should be checked; the intended terminology appears to be serum amyloid A.

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6. The conclusion should be more cautious. The statement supporting integration of SAA into routine practice should be qualified because the manuscript itself identifies assay standardization and disease-specific reference ranges as unresolved issues.
7. Reference formatting should be carefully standardized according to the journal's required style.

Overall Assessment

The manuscript addresses an important and clinically relevant biomarker and provides a useful overview of the biochemical, physiological, and clinical aspects of SAA. The overall structure is acceptable, and the topic has potential significance. However, scientific claims need better qualification, factual inconsistencies need correction, references require verification, and substantial language editing is necessary.

Recommendation: Accept after major revision.