Reviewer’s report

Title: Shine & Lal index as a predictor for early detection of β-thalassemia carriers in a limited resource area in Bandung, Indonesia

Version: 0 Date: 04 Mar 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?
Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
No - there are minor issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?
No - there are minor issues

Statistics - Is the use of statistics in the manuscript appropriate?
No - there are issues with the statistics in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
No - there are minor issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?
Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: This is a well conceived, but poorly executed study, aiming to investigate the utility of several full blood count metrics in the screening of beta-thalassemia carriers, in a region where molecular methods are not readily available. Unfortunately, due to logistical and fination limitations (recognised and discussed in the manuscript) the data was not conclusive. Also, the use of language and non-standard gene nomenclature further hamper what could otherwise be an interesting (if minor) addition to the field.
REQUESTED REVISIONS:

General comments:
HGNS nomenclature must be used for all gene names and HGVS nomenclature should be followed for the description of all variants; the legacy nomenclature currently used can be added in parenthesis on first use, e.g.: HBB c.93+1G>T (IVS1nt1). The transcript accession number used for the analysis should also be given on first use, e.g., for HBB, NM_000518 should be given if used.

Syntax, grammar and other typography are not to required standard; must recruit editorial input from someone necessarily proficient in English.

Specific comments:
Page2Line8: is 'thalassemia' a single gene disorder? This could cover both a- and b- thalassemia, which affects two gene loci; please specify b-thalassaemia in this context and elsewhere in the text).
P2L15: should be: 'not yet mandatory'. Also, is mandatory the word the authors are looking for here?
P3L19: there should be discussion about the genetics of b-thal, inheritance patterns and difference between (in terms of clinical severity) of the carrier (trait) and disease (biallelic) states.
P3L29: mean what? (MCH); also, laboratory, not laboratorium. Also, there should be a description of how the various blood count metrics relate to b-thalassemia and how these are used for a differential diagnosis. Simply linking to references is not sufficient - do not assume expert-levels of knowledge in the prospective readership.
P3L41: haemoglobin E, not haemoglobinopathy E?
P4L22: need to introduce the concept of HBB pathogenic variants, gene structure and association with disease phenotype before discussing actual variants. These should also be defined according to HGVS nomenclature.
P4L36: HBB gene; also, do the primers used span the whole gene (including 5' and 3' UTRs and introns)? Unless commercially sensitive, the primer sequences should be given (along with any references relating to design & validation).
P5L39: there is no Figure 4…
P6L21: 57.1% is not a small percentage!! 25.9% is not a 'small' percentage either… this line of argument must be reframed to reflect the data.
P6L51: 'some machines'…? Do the authors mean capillary electrophoreses platforms? Please use precise technical language.
P7L16: first mention of a-thalassemia, this - and similarities and differences with b-thal - should have been introduced in the Introduction.
P7L29: what do the authors mean by 'towards zero birth of thalassemia'? The authors should think very carefully about the implications of this statement and either clarify or remove.
P7L31: the lack of pedigree data to establish genotype/phenotype segregation is a fairly major issue with this study; citing 'lack of time' is not acceptable for a scientific study.

ADDITIONAL REQUESTS/SUGGESTIONS:
None in addition to above

Note: This reviewer report can be downloaded - see attached pdf file.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

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