

ANSWERING REVIEWERS

Dear Editor,

Please find enclosed the edited manuscript in word format (file name: 21530-Review.doc).



Title: Universal screening for hemoglobinopathies in today's multi-ethnic societies: How and when

Author: Piero C Giordano

Name of Journal: *World Journal of Obstetrics and Gynecology*

ESPS Manuscript NO: 21530

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer:

Please find hereby the revised manuscript with all changes highlighted as requested. Comments of the referees have been processed as follows:

Reviewer 1 (00452844)

C: This is an interesting review article on screening for Hemoglobinopathies.

R: Thank you for the words of appreciation.

C: The author states that screening for these conditions early in pregnancy should be added to the routine screening. A point, however, that should be added is that pre-pregnancy counseling and screening might be more suitable, since this gives the opportunity for pre-pregnancy diagnosis in the pre-embryo before implantation via the pre-implantation genetic diagnosis.

R: The author agrees with this comment which is valid for societies in which an organized HBP management exists. Nevertheless, pre-pregnancy counseling is not available in many countries and in particular in non-endemic immigration areas where HBP's are still considered an import disease and where little awareness is present in the daily healthcare structures and in the public. Putting up such a structure would take many efforts, lot of time and money while Rhesus screening is there and working at low cost. Regarding PGD, most countries offer this only in case of fertility problems and/or embryo selection when a suitable stem cells donor is needed for an affected child. All this has been specified in the revised version.

Reviewer 2 (00742368)

C: Very interesting topic. I personally enjoyed reading this reminder of basic diagnostic dilemmas in Hemoglobinopathies.

R: Thank you for the words of appreciation and for providing an attachment with editorial comments and language improvements on the manuscript.

C: The main issue in this article-despite the enthusiastic tone- is that the author did not prove the cost-effectiveness of screening with HPLC or CE nor did he comment on the sensitivity and specificity of different screening strategies.

R: It is common knowledge that HPLC screening for HBP is the most sensitive, (provisionally) specific and economically convenient method (references provided). The methods are applied for newborn screening world-wide, with early treatment as only direct benefit. When applied to primary prevention the cost versus effectiveness is evident as the cost of a life time treatment of a single patient is astronomical (reference provided). Sentences have been included to explain this more clearly.

C: I have enclosed some editorial comments and changes on the original manuscript.

R: Thank you again for your kindness.

C: Finally, I would be interested in seeing a flow diagram of this screening method

R: Good idea, a flow diagram has been included in the revised version.

3 References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Obstetrics and Gynecology*.

Thanks and kind regards,

Piero Giordano