Dear Lian-Sheng Ma,

Company Editor-in-Chief,

Baishideng Publishing Group Inc,

Thank you for your mail dated 2020-03-24,

We revised our Manuscript NO.: 53758 entitled "Antiphospholipid syndrome and its role in pediatric cerebrovascular diseases: a literature review", submitted to World Journal of Clinical Cases which was offered for initial acceptance for publication in the WJCC.

According to the reviewer comments we provided a point to point response. We highlighted all corrections suggestes by reviewers or additional text in red. The manuscript was also improved by a native speaker.

Thank you very much for your efforts in processing of our manuscript.

Sincerely yours,

Beata Sarecka-Hujar, PhD

Ilona Kopyta, MD, PhD

RESPONSE TO REVIEWS:

Reviewer 1:

03546728 Conclusion: Rejection

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

This review is well written and is a clear summary of APS in children. However, I don't see what is new in your study compared to recent studies such as : Pediatric APS: State of the Art. Soybilgic A, Avcin T. Curr Rheumatol Rep. 2020 Mar 3;22(3):9. or Pediatric antiphospholipid syndrome. Madison JA, Zuo Y, Knight JS. Eur J Rheumatol. 2019 Dec 3:1-10. Can you justify?

Reply:

Thank you very much for your evaluation. We were built up with your comment that our manuscript was well written. As for the comment that there is nothing new when compared to the previously published reviews we would like to explain that when we submitted this manuscript for evaluation in WJCC, the publication by Soybilgic and Avcin was not published yet, so we could not know what content is inside. In contrast to Madison's review, our manuscript contains an analysis of possible interactions between selected candidate genes and the APS syndrome/the presence of aPLs in the pathogenesis of cerebrovascular disease in children.

In addition, after a long discussion, we have decided to include a section with exhaustive analysis on relations between APS and the risk of recurrence of thrombotic events.

The language of the manuscript was also improved by a native speaker.

Reviewer 2:

00068912 Conclusion: Minor revision

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Name of journal: World Journal of Clinical Cases 53758. Review Dear Lian-Sheng Ma, Founder and Chief Executive Officer.

1. The topic of this review falls within the scope of "World Journal of Clinical Cases". The manuscript entitled “Antiphospholipid syndrome and its role in pediatric cerebrovascular diseases: a literature review” by Sarecka-Hujar B., Kopyta I. is devoted to the manuscript is devoted to the description of the literature data on the development of venous and arterial thrombosis as well as ischemic strokes during the characteristic clinical picture of AFS in the child population. The Authors this review tackles a very interesting clinical problem. The Title of manuscript reflects the content of the article. The writing up of the abstract meets the journal requirements. The Abstract shows all the sections that have been studied and reported in the review. In line 4 of the abstract, "β2 GPI" should be replaced with "anti-β2GP-1" (and throughout the text to present the same).

Reply:

Thank you very much for this comment. We have unify and corrected the name of "anti-β2GP-1" throughout the whole text. The language of the manuscript was also improved by a native speaker.

2. The Introduction exposes the most evident data known on Antiphospholipid syndrome in pediatric and in adults. The all this gives sufficient information about the research objective. In this study by authors present data on diagnostic criteria of APS; role of aPLs in thrombotic events; epidemiological data on APS in adults and children; clinical presentation, other than cerebrovascular, of APS in pediatric population; cerebrovascular disorders in children with APS, treatment of APS in pediatric population. The authors describe the role of antiphospholipid antibodies in the formation of thrombosis. In the pathogenesis of thrombosis in APS, the entire hemostatic system is affected (Reshetnyak V.I., Maev I.V., Reshetnyak T.M., Zhuravel S.V., Pisarev V.M. Liver Disease and Hemostasis (Review) Part 2. Cholestatic Liver Disease and Hemostasis. General Reanimatology 2019; 15(6): 80-93. DOI:10.15360/1813-9779-2019-6-80-93). Among the mechanisms of development, an important role belongs to the reduction of fibrinolysis (Aisina R.B., Mukhametova L.I., Varfolomeyev S.D., Ostryakova E.V., Seredavkina N.V., Reshetnyak T.M., Nasonov E.L., Patrushev L.I., Patrusheva N.L., Gulin D.A., Gershkovich K.B. Polymorphism of the plasminogen activator inhibitor type 1 gene, plasminogen level and thromboses in

patients with the antiphospholipid syndrome. Biochemistry (Moscow) Supplement. Series B: Biomedical Chemistry. 2013;7 (1):1-15. PMID: 24749249. DOI: 10.18097/pbmc20146001072). Genetic polymorphism of genes in the hemostasis system is a condition in which the failure of genes can occur under certain trigger factors. Mutations in the V and II blood factor genes are associated with venous thrombomboembolic complications. There are a number of descriptions of cases where these mutations are combined with antiphospholipid antibodies and thrombotic complications. Mutations in the 5.10 methylentetrahydrofolate reductase gene can lead to hyperhomocysteinemia and thrombotic complications. The risk of developing thrombosis increases when the polymorphism of these genes is combined with antiphospholipid antibodies (Reshetniak TM, Patrushev LI, Tikhonova TF, Kovalenko TF, Mach ES, Aleksandrova EN, Miroshnikov AI, Nasonova VA. [Mutation of a 5,10-methylenetetrahydrofolate reductase gene in systemic lupus erythematosis and antiphospholipid syndrome]. Ter Arkh. Russian. 2002;74(5):28-32. PMID: 12087901) Conclusion summarizes the most evident data collected by the review and presented. In summary this work is well performed.

Reply:

Thank you very much for your kind evaluation. We have addedd the proposed references into the discussion on the relationships between genetic polymorphims of candidate-genes and APS in pathogenesis of cerebrovascular disease in children. We have also enriched our literature review with the new chapter concerning the role of APS in the occurrence of subsequent thrombotic events in children. Studies on recurrent thrombotic events, including AIS in children with APS, are scarce. This is due to the rarity of cooccurrence of these disorders in pediatric patients. In turn, in a situation where recurrences of thrombotic events are even rarer pediatric APS with subsequent AIS is extreme rare.

Reviewer 3:

03254239 Conclusion: Accept (General priority)

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

The authors have written a nice review on Antiphospholipid syndrome and its role in pediatric cerebrovascular diseases. The authors have done a useful literature review. The manuscript is nicely written.

Reply:

Thanl you very much for these kind comments. We have enriched our manuscript with a chapter concerning the role of APS in the occurence of subsequent thrombotic events, including arterial ischemic stroke in children as well as we have added some information in the section analyzing relationships between APS and genetic polymorphisms in cerebrovascular diseases in children (please find added paragraphs marked in red color through the text).

The language of the manuscript was also improved by a native speaker.