

We thank the reviewers thoughtful and insightful comments and suggestions. We have addressed all of these. The resulting modified manuscript has benefited from these additions and we believe it is worthy of publication in the World Journal of Gastroenterology due to its novelty and scientific merits.

Detailed response to referee's comments:

Reviewer #1 (Remarks to the Author):

They are the first to demonstrate that the mode of delivery influences the frequency and functionality of CD71+ erythroid cells in both cord blood and placenta tissues. There is no doubt; those findings are of outstanding importance. Figures are of good quality and very illustrative.

I appreciate the reviewers' encouraging comments.

1. Please explain why you consider this a case control "STUDY".

Because it was a case report, I thought "case control" might be the most appropriate article type however Associate editor may modify it appropriately.

2. Please insert "Core tip" and "Key words" in the manuscript, not only on the submission site.

I appreciate the suggestion and in agreement Key words and Core tip are included in the title page. Audio Core tip is also provided.

3. Please correct "ulceraitive" in the key words. Please insert the full verb in "however their frequency and function in vaginal versus C-section deliveries of full-term pregnancies in particular in inflammatory bowel disease (IBD) patients yet to be determined".

Thanks for suggestion and these are corrected.

4. The following sentences should not be in the Introduction, since they represent the description of presented cases. "Twin A was born by naturally induced vaginal delivery, the other twin by urgent C-section which is commonly practiced in order to reduce stress for the second twins 16 or due to delivery associated complications. In this case, the head of baby B was high and variable uncomplicated fetal heart rate decelerations was noted. As the head was descending the cervix did clamp down, at that point urgent C-section was recommended."

Thanks for the suggestion. These sentences were removed from the introduction and included in the materials and methods section as "case description".

5. Conclusion of the study should not be in the Introduction:

"Our findings suggest mode of delivery directs immunological changes which may have potential long-term effects on the offspring."

I appreciate the suggestion, in agreement with the reviewer's suggestion this sentence has been removed and included in the conclusion section.

6. Material and methods should be re-written, with proper description of cases there.

I appreciate the recommendation and in agreement we have included the case description in materials and methods section. We have also included the exact delivery time for baby A and baby B.

7. The following sentence should be moved from "Results" to "Methods": "CBMCs were freshly isolated from cord blood of the newborns and immune phenotyping was performed for the frequency of different immune cells such as T cells, NK cells, monocytes, CD71+ erythroid cells and neutrophils".

CBMCs isolation was already included in the results section. Thus, we modified this sentence in agreement with the reviewer's suggestion.

8. "Results" should include only the findings from the presented cases. Comparisons with other studies from the literature should be made in the "Discussion". Here and there, the comparisons with other studies are redundant in the "Results" and "Discussion". They should be carefully reviewed.

I appreciate the suggestion however some journals allow inclusion of references in results section. I did not observe any restrictions by the WJG in this regard. I don't see this as a major problem but might be helpful to the readers.

9. The main text is not written according to the Format style indicated by the WJG.

Thanks for the suggestion. We have extensively modified the text including references to meet the WJG requirements.

10. Table 1A needs reformatting.

The table 1A is reformatted now.

11. References are not written according to the requirements of the WJG, otherwise they are pertinent.

Thanks for the reminder. As I mentioned above references are modified to the requirements of WJG.

12. Why did the researchers choose to test fecal calprotectin at 12 weeks after delivery?

This was the only time point fecal samples were submitted.

13. The authors could insert more clinical data about the two twins: growth, TYPE OF FEEDING, stools/day etc. Were they both in good health? Fecal calprotectin values in little infants are generally higher and 982 could be a normal value. Fecal calprotectin can be as high as 2000 in healthy breastfed infants (Savino et al, 2010).

We appreciate the suggestions. We have discussed the FCP levels in healthy infants by referencing the article by Savion et al. Until 12 weeks of age both infants were in good health and had similar weight gain trend. This is included in Clinical observations of the mother, infants at delivery and 12 weeks of age

Reviewer #2 (Remarks to the Author):

The authors of this manuscript brilliantly investigated immunological differences in cord blood and placenta of twins, of which one was delivered by vaginal and the other by urgent C-section. A trend in reduction of T cells, monocytes and neutrophils was observed in the cord blood of C-section delivered versus the vaginally delivered twin. This is in line with other reports indicating that C-section newborns have lower leukocytes count in their cord blood. I think the article is well written and results are sounding.

We appreciate the support and positive impression by the reviewer on our manuscript.

I found that the discussion of the confounding factors is poor (e.g. the time of the urgent C-section may be crucial and may influence the immunity of the offsprings).

We appreciate the important comment and in response we have provided this info in the case description section and also in the discussion. In fact, the child B was delivered 37 min later by C-section.