GOCM Gynecology and Obstetrics Clinical Medicine

PEER REVIEW HISTORY

Gynecology and Obstetrics Clinical Medicine publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Prediction of neonatal acidemia at birth with intrapartum total deceleration area on fetal cardiotocogram
AUTHORS	Khursheed, Romana; Vimalesan, Eniya; Maldar, Arif; Dalal, Anita; Vyshnavi, Korpala

VERSION 1 - REVIEW

REVIEWER NAME	***Geva, Neta***
REVIEWER AFFILIATION	
REVIEWER CONFLICT OF INTEREST	No competing Interest
DATE REVIEW RETURNED	14-Oct-2024

GENERAL COMMENTS	This study aims to analyze the association between total deceleration area on electronic fetal monitoring 30 minutes prior to delivery with a arterial cord pH less than 7.2. this work adds to a body of knowledge already published on this issue, in a specific population that is underreported in these studies. This study holds importance but needs to be revised and improved in both it's result presentation and relevance of discussion before it is publishable. General comments: 1. "Fetal cardiotocography" is wrong term as the tocography=refers to the uterine contractions. The correct terms would be one of the following "intrapartum cardiotocography", "cardiotography", "electronic fetal monitoring". Please choose the appropriate term for you and use a correct one. 2. Using a pH of 7.2 is probably not an appropriate clinical delineator, and if a target of pH above 7.2 would be an indication to for a ceserean we would probably doing more damage than good. Some (Matmor et al. Int J Gynaecol Obstet. 2022 Dec) have used 7.1 and there would be clearer indication to use 7.0 as this is associated with neonatal encephalopathy, the use of 7.2 is more for stasistical reasons and there the AUC cutoff shouldn't be used. This issue is a main limitation of this work, as well as many others in the field and should be properly discussed. 3. Is there any data on actual outcomes, this has not being discussed at all. TDA has been associated with HIE (Geva Y et al. Int J Gynaecol Obstet. 2023) and with specific MRI findings (Geva N, et al. Pediatr Res. 2023) these are in turn are associated with but not equal acidemia.

	4. There is a misunderstanding of what the inclusion and exclusion criteria are of this work, what does screen for eligibility mean, and how were there deemed eligible, the inclusion criteria were term singleton – therefore preterm baby shouldn't have been included in the first place. 5. Why choose 30 min (see above references) any clinical reason? Please explain or discuss decision that is different to Cahil et at, Furukawa et al, Geva et al Specific comments: Abstract: 6. Please avoid using acronyms in the abstract, or if using them – explain them in the first time used (TDA) 7. Line 42 "intrapartum fetal distress -how was it diagnosed (for example – do you mean NIHCD category II/III?) 8. Line 44 What does prior do decision to delivery mean? 9. Do you think that pH<7.2= fetal acidemia? If so please reference, do you think that this is the relevant number, if so please explain and reference. 10. TDA – explain here Introduction: 11. Line 20: are most fetal distresses managed by CS, are there numbers/references for this claim, are there criteria for this? 12. Line 21: "exponential" please drop this word; this is a mathematical term and not what you meant. 13. Line 23: by "primary" did you mean emergent? Please correct or explain. 14. Lines 52-55: this is a very problematic claim to make that I suggest deleting and rephrasing. Do not claim that it is used for "medicolegal" rather than medical reasons, as this is a preposterous claim about your own practices (this is after all a single centre study). 15. Page 6 line 5: "prevention" or diagnosis? Material and methods: 16. The Material and methods section is missing many terms used later in the paper, please see specific comments of the results and discussion. 17. Intrapartum fetal distress: how was the diagnosis made (NICHD category II/II tracing? By whom) this needs to be elaborated. 18. Cord gases: taken by whom, do you take venous gases as well? 19. Lines 44-50: this paragraph is unclear to me, were the laboring mother under continuous monitoring or was there intermittent monitoring – this is unclear and needs to be rephrased. 20. Page 8 line 9: what was the time between the decision to go for a cesarean delivery to the actual surgery? Was this measured? What is the implications of this (discussion) 21. Sample size: without reviewing the numbers – the required number was somehow exactly the number of eligible neonates in a period of exactly 12 months? Results: 22. "screened for eligibility" needed an explanation in the methods. 23. Neonatal acidemia – please use "neonates with cord pH<7.2" instead. 24. Lines 51-54 please rephrase unclear sentence about primigravida. 25. Page 12 line 14: "beat to beat variability" is missing from the methods. 26. Line 16: "late deceleration" missing from methods.

	27. Mann Whtney… belongs in methods 28. Measure in the tables, are missing from methods and need an explanation. 29. NICU admissions is a problematic measure – what are the indications for admission – is acidemia an indication? What level? Discussion: Please see general comments 30. Numbers throughout this section need units. TDA is presented interchangeably as missed beats (not explained in methods or into) and cm2. 31. “missed beats” is a new term here, not in the methods and not referenced. 32. “high risk population” what high risks are included? Are the same criteria valid for the different populations? (meconium Matmor Loeub et al, IUGR – Geva et al) 33. Page 17 line 21: postdatism was never defined, what are the recommendations and management criteria for this population, please discuss their possible different criteria and different management, consider excluding from analysis 34. Line 33: what the indications for induced labor? Do they include mild fetal distress? 35. Page 18 line 19: outcomes were not discussed anywhere in this paper. A pH of any value is a lab value that is possibly associated with an outcome (needs to be discussed and referenced). Conclusion: 36. As noted above, please do not recommend using an ROC curve to avoid any pH<7.2 as this will lead to further increase of unnecessary cesareans, rephrase conclsusion. Tables: 37. All table require a legend and an explanation to all acronyms used in the table. 38. There is no need to say “yes” and “no” to every variable, it is redundant, and column 2 of most tables shou be taken off – for example Fetal tachycardia (%) / 8(19.05) / 30(23.81) / 0.0082.

REVIEWER NAME	***Cavoretto, Paolo***
REVIEWER AFFILIATION	
REVIEWER CONFLICT OF INTEREST	No competing Interest
DATE REVIEW RETURNED	19-Oct-2024

GENERAL COMMENTS	Despite this method is not novel and other major works, partly cited by the authors exploded this approach, the study aim and topic is interesting and deserves to be moved forward in the editorial process. Infact, the article has the merit to present scientifically sound methodology and a robust rationale with an original view of CTG analysis. I have some reccomendations and constructive criticisms for the authors to mimprove the article: Major comments 1. A method for prospective application of this method should be described, otherwise it remains a mere speculation on retrospective data of already delivered cases. The difficult and challenging application of CTG is due to the need of the real-time management for each modification of the trace. Do they think that may be possible creating stages of alert, based on the TDA? (E.g., early, intermediate and late anomalies or low-intermediate and high risk?)

	2. A picture would be highly beneficial to show graphically how the area under the CTG trace is calculated. 3. Our group published that the risk of neonatal acidemia is directly proportional to duration of the 2nd stage of labour. This is a very relevant clinical feature and the same area (or area decrease) may be distrubuted in different second stages durations showing different clinical impact. I am aware that here the authors are analysing only 30 minutes however this is difficult to apply in a prospective use, as the final duration of the second stage is not certain until the first fetal shoulder is extracted. Please the authors consider this variable or disclose this limitation, adding a brief discussion on this essential topic in the comment section along with major references. (ref 1-2) 4.Umbilical cord metabolic acidemia at birth (MA) is generally defined with umbilical artery pH < 7.0 and/or BE ≤ − 12 mmol/L (ref 3). Were the authors aligned with these criteria? 5. Has Tachicardia the ability to increase deceleration area over the baseline? Has mild bradycardia (e.g., 110 bpm) the ability of decreasing TDA?? Are these modifications clinically relevant (impact of pH, BeB)? In other words for similar area TDA is the pH different when higher or lower baselines are found? This can be done within a multivariable statistical approach. 6. Effect of other covariates should aldso be explored if possible within the LR model, if not please disclose in the limitation section their effect (FGR, PE, oligoamnios, epidural/neuraxial analgesia, parity, etc) References 1. Cavoretto PI, Seidenari A, Amodeo S, Della Gatta AN, Nale R, Ismail YS, Candiani M, Farina A. Quantification of Posterior Risk Related to Intrapartum FIGO 2015 Criteria for Cardiotocography in the Second Stage of Labor. Fetal Diagn Ther. 2021;48(2):149-157. doi: 10.1159/000512658. Epub 2021 Jan 28. PMID: 33508830. 2. Cavoretto PI, Seidenari A, Farina A. Hazard and cumulative incidence of umbilical cord metabolic acidemia at birth in fetuses experiencing the second stage of labor and pathologic intrapartum fetal heart rate requiring expedited delivery. Arch Gynecol Obstet. 2023 Apr;307(4):1225-1232. doi: 10.1007/s00404-022-06594-1. Epub 2022 May 21. PMID: 35596749; PMCID: PMC10023766. 3. (2014) Executive summary: Neonatal encephalopathy and neurologic outcome, second edition. Report of the American College of Obstetricians and Gynecologists' Task Force on Neonatal Encephalopathy. ObstetGynecol 123:896–901.

VERSION 1 – AUTHOR RESPONSE

VERSION 2 – REVIEW

REVIEWER NAME	***Geva, Neta***
REVIEWER AFFILIATION	
REVIEWER CONFLICT OF INTEREST	No completing interest
DATE REVIEW RETURNED	24-Nov-2024

GENERAL COMMENTS	I am satisfying that the manuscript has been reviewed and changed appropriately and is definitely "worth" a place in your papaer

REVIEWER NAME	***Cavoretto, Paolo***
REVIEWER AFFILIATION	
REVIEWER CONFLICT OF INTEREST	No completing interest
DATE REVIEW RETURNED	24-Nov-2024

GENERAL COMMENTS	The revision was successful (most issues resolved or explained) and the article may be published

VERSION 2 – AUTHOR RESPONSE