Reviewer's report

Title: Foetal aortic flow velocity waveforms in healthy and hypertensive pregnant women

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Reviewer: Francesco Stea

Reviewer's report:

- Major Compulsory Revisions

1- Abstract, Conclusions: this does not seem the main finding. I would say that the main finding is that pulsatility indexes trend up during pregnancy in both normotensive and hypertensive women. The increase could be said to be less pronounced only if a formal statistical comparison is performed (see further on).

2- Results: The study is a comparison between normotensive and hypertensive women, but blood pressure is not reported. If the BP difference between groups is small, it could explain the non-significance of difference in results with this number of subjects.

3- It is hard to infer curves, especially curves other than a straight line, from three points only.

Using the log of time in the analyses, rather than the time, may seem artificial.

The authors should clarify why they choose a non-linear relationship and why they opted for log-transforming the time.

It is not even clear if “time” in the analyses refers to trimester 1-2-3 or to the exact gestational week. In the first case, it would be hard to treat it as a continuous variable, not to mention log-transforming it.

4- Results, multivariate analysis / Figure 3: it is hard to infer from figure 3 that RI is different between HT and NT. No p-value is mentioned. See also comment in the next section.

No statistical analysis and p-value are shown to support the statement that the curves and the evolution over time are significantly different and different from a flat line.

5- Discussion, page 12, second paragraph: no formal statistical analysis was performed to say that the PI trends are divergent.

6- Even assuming that the trends are significantly divergent, since PI and RI do not reflect arterial impedance only, but depend on several factors – as the authors have correctly stated – I would soften statements in the patho-physiological explication, and above all I would not attribute the changes to the aorta only.

7- Conclusions: as said above, this does not seem to be the main finding of the study; no formal statistical comparison was performed to say that trends are
different; it is hard to conceive that adaptive mechanisms would be “local” and selectively concern the aorta only.

• Minor Essential Revisions

8- Abstract, Background: “aimed to compare” -> “aimed at comparing”
9- Throughout the abstract and the manuscript: “indexes” and “indices” are both acceptable, but you should stick to one form.
10- Introduction, first paragraph: “It’s application”… The period is not clear, there are probably some misspellings. Could “It’s” be “Its”?  
11- Paragraph two: “foetal circulations because they” -> “foetal circulations, because they”
12- Third paragraph: Resistance and pulsatility indexes should both begin either with upper or lower case letters.
13- Page 4, last paragraph: i would use “chronic arterial hypertension” rather than “chronic hypertension”.
14- In a medical context I would say “a highly prevalent disease” rather than “a prevalent disease”.
15- Page 5, first line: “impinge enhanced risk” -> “impinge on the risk”
16- Last paragraph: “we aimed in to compare” -> “we aimed at comparing”. See above for “indices”.
17- Patients and Methods: Acetylsalicilic acid is not entirely neutral to hemodynamics or maternal biochemistry, even at low doses. Since women taking this drug were included, this subject is to be discussed. If all hypertensive and no normotensive were taking the drug, this should be clearly stated; if the proportions are different from 100 and 0% respectively, they should be reported and used as confounders in the analysis.
18- Patients and Methods, Subjects, paragraph two: “taking other medication” -> “taking other medications”
19- Paragraph three: a comma should be placed after “the first ultrasound evaluation”
20- Page 6: “which corresponds closely to” -> “which corresponds _quite_ closely to”
21- If growth <10th or >90th percentile is an exclusion criteria, it should be stated previously rather than here. Note that it excludes nearly 20% of pregnancies: the number of subjects excluded due to this criteria should be stated. It is not clear if this is actually an exclusion criteria at baseline and/or a reason for quitting the follow-up. Please make more clear.
22- Page 6: numbers about follow-up and exclusions – actually more a dropout – should go in the Results section.
23- Patients and Methods, Clinical data..., first paragraph: since a trimester is too long, weeks chosen for evaluation should also be provided.
24- Results, first paragraph, and Table 1: it is questionable to report and compare age and BMI as intervals rather than mean and SD if normally distributed or median and interquartile range if not.

25- Results, first paragraph: the sentences about the age of the population and the mean gestational age at birth are a duplicate of the data in the table so they should be omitted, or different information could be conveyed here.

26- Results / Table 2 / Figure 2: Table 2 and Figure 2 partially show the same data, so they are redundant. My suggestion is to show data with figures only (and possibly to write means and SD in the context of the graph) marking significant differences between groups.

27- Page 10, last line: “puts impedance data at a lower level” is not clear.

28- Discussion, page 11, last paragraph: the sentence about foetal stimulation and maternal mobilization should be in the Methods section.

29- Page 12, first paragraph: since no analysis was performed on the fluxometric spectra themselves, the sentence about them should be omitted or softened to “no GROSS morphological differences were identified”.

30- Table 1: as already said, “pregnancy outcomes” is probably not a correct term; age and BMI would better be shown with numbers rather than intervals.

31- Table 2: as already said, I would merge it with figure 2. If the table is maintained, significant differences should be marked.

32- Table 3: it is not clear what the “expected indices” are. Is it RI?

As PI and RI are so highly correlated, it makes little sense to put PI into a multivariate model for RI.

If * is used to multiply, it can’t be used to mark a significance, and vice versa. A “x” could be used for multiplications.

33- Figure 3: as already said, significant differences should be clearly marked. This kind of graph can’t anyway used to show differences between HT and NT.

• Discretionary Revisions

34- Please use the same format for all author affiliations (some have the full address, some do not include the country…)

35- The word “index” is repeated several times; synonyms could be used.

36- Introduction: “intra uterine” should better be spelt “intrauterine” or “intra-uterine”.

37- Patients and Methods, Subjects, paragraph two: the number of recruited subjects should be in the Results section.

38- “We studied women… hypertension” -> “We studied singleton pregnancies in healthy women or in women with chronic arterial hypertension”
39- Patients and Methods, Statistical analysis: I would not call “standard” the statistical methods that are rather “appropriate”, neither call “usual” the p-value of 0.05.

40- Results, first paragraph, and Table 1: the term “pregnancy outcomes” to refer to GA at examination and delivery only is questionable.

41- Figure 2: box-and-whiskers plots are preferable to histograms here.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests