**An Overview of Oxidative Stress and Its Effect on Fetal Development and Organogenesis**

The review “An Overview of Oxidative Stress and Its Effect on Fetal Development and Organogenesis” provides a clear overview of Reactive Oxygen Species (ROS) with emphasis on its effect on fetal development and organogenesis. ROS are involved in the etiology of numerous other diseases including cardio-vascular diseases, diabetes mellitus, ischemic diseases and aging processes that are highly prevalent in Asian countries. Hence the review of this paper is relevant, timely, and of interest to the audience of this journal. It also provides treatment plan required for abnormalities related to fetal development.

The review is well written and several points that strengthen this article are,

1. The content of this review is technically accurate and sound.

2. The abstract is concise and sufficient. Please remove the word “paper” in the sentence “In this review paper, we will address the generation of pro-oxidents, its normal physiological role in intra-uterine environment establishment in placenta and in case of excess OS, its detrimental effects on fetal development and organogenesis”

3. The introduction provides the necessary background information. However, a couple of paragraphs from other sections need to be moved to the introduction section.

4. The review is easy to read and free from grammatical or spelling errors.

5. The review clearly highlights and suggest that hypoxia, oxidative and nitrative stress alter placenta development and may be a general underlying mechanism that links altered placental function to fetal programming.

However, the authors need to address the below points that would further strengthen the review article.

1. The authors need to shorten extensively the review article excluding the introduction. Currently the review is elaborate with too many non-essential referenced articles.

2. The review will greatly benefit if the authors can provide a table describing the side effects ROS on fetal growth. This will greatly reduce the review section.

The review can be concised with an example suggested below,

a. In section 2, the below two paragraphs can be briefed in a 1-2 sentences.

“One of the major ROS is nitric oxide (NO) which is a free radical with vasodilatory properties and is an important inducer of cell signaling pathways involved in many physiological and pathological processes [28]. It can be produced by 3 types of nitric oxide synthase (NOS) isoenzymes in mammals, named neuronal NO synthase (NO synthase 1), inducible NO synthase (NO synthase 2) and endothelial NO synthase (NO synthase 3) [29].

Neuronal NO synthase (nNOS) and endothelial NO synthase (eNOS) are constitutive. Mononuclear phagocytes (monocytes and macrophages) produce a large amount of inducible NO synthase (iNOS). iNOS is expressed in response to pro-inflammatory cytokines and lipopolysaccharides [19,30,31]. During the follicular development, eNOS is expressed in granulosa cells and the surface of oocyte. In most organs, iNOS is expressed in response to immunological stimuli [32] but in pathological conditions, it might play a major role in NO production”

b. Similarly all the remaining sections 3, 4 and 5 need to shortened. Also please discuss only very essential reference articles.

3. Currently there are around 190 references which can be reduced to 150 and below after reworking on the various sections.

4. There is evidence that several teratogens affect the developing embryo by increasing its oxidative stress and, because of its relatively weak antioxidant defense, especially at the early stages of organogenesis, result in severe embryonic damage. The authors need to give a brief explanation about the teratogens in the introduction section rather than mentioning in the conclusion section.

5. The introduction section has only couple of sentences describing about the genetic factors. Many studies have shown “The ability of the developing embryo to cope with oxidative stress largely depends on its antioxidant capacity that is determined both by embryonic age at injury and by genetic factors dominating the endogenous antioxidant capacity.” Please add a couple more sentences on the importance of genetic factors contribution.

6. Please add a couple more sentences on the importance of non-toxic antioxidants and how they might prove a very efficient and inexpensive way to reduce the rate of very disturbing congenital anomalies.

The authors need to address these minor comments before the review can be considered for publication.