



OPEN ACCESS

EDITED AND REVIEWED BY
Wei Ge,
University of Macau, China

*CORRESPONDENCE
Jayonta Bhattacharjee
✉ bhattacharjee@bau.edu.bd

RECEIVED 03 April 2024
ACCEPTED 23 April 2024
PUBLISHED 13 May 2024

CITATION
Bhattacharjee J, Rolfo A, Barbosa BF,
Imakawa K and Ermini L (2024) Editorial:
Developmental biology and endocrine
research for a successful pregnancy.
Front. Endocrinol. 15:1411864.
doi: 10.3389/fendo.2024.1411864

COPYRIGHT
© 2024 Bhattacharjee, Rolfo, Barbosa, Imakawa
and Ermini. This is an open-access article
distributed under the terms of the [Creative
Commons Attribution License \(CC BY\)](#). The
use, distribution or reproduction in other
forums is permitted, provided the original
author(s) and the copyright owner(s) are
credited and that the original publication in
this journal is cited, in accordance with
accepted academic practice. No use,
distribution or reproduction is permitted
which does not comply with these terms.

Editorial: Developmental biology and endocrine research for a successful pregnancy

Jayonta Bhattacharjee^{1*}, Alessandro Rolfo²,
Bellisa Freitas Barbosa³, Kazuhiko Imakawa⁴
and Leonardo Ermini⁵

¹Department of Surgery and Obstetrics, Bangladesh Agricultural University, Mymensingh, Bangladesh, ²Department of Surgical Sciences, School of Medicine, University of Turin, Turin, Italy, ³Laboratory of Immunophysiology of Reproduction, Institute of Biomedical Science, Federal University of Uberlândia, Uberlândia, Brazil, ⁴Research Institute of Agriculture, Tokai University, Kumamoto, Japan, ⁵Department of Life Sciences, University of Siena, Siena, Italy

KEYWORDS

pregnancy, placenta, trophoblast, developmental-biology, endocrine-research

Editorial on the Research Topic

Developmental biology and endocrine research for a successful pregnancy

Pregnancy is central to mammals' lives, growth, and development. A healthy pregnancy is not only a prerequisite for a species' survival and existence but also crucial for the growth and development of livestock and agriculture sectors, such as dairy and beef animals. Pregnancy failure and fertility have long been studied in developmental biology and endocrinology, and new inventions and technologies are welcome in this field.

Many factors, including endocrine disruptors and sedentary lifestyles, are becoming more prevalent in modern culture, limiting and impeding pregnancy success. Thus, reproductive development, endocrinology, and infectious mechanisms in pregnancy must be understood. Proper knowledge of reproductive development and endocrinological techniques will enable us to develop strategies to mitigate the pathologies and factors affecting a successful pregnancy.

Multiple reproductive organs regulate developmental biology. Starting from external and accessory reproductive organs, the uterus, oviduct, ovaries, and their health and optimum function are prerequisites for a successful pregnancy. Along with the reproductive organs, many other factors also regulate pregnancy success. Lifestyle factors, such as physical activity, good nutrition, and exposure to endocrine disruptors, influence reproductive and developmental outcomes. Knowing about all disorders and conditions affecting reproductive development and their management is crucial.

The objective of the Research Topic "*Developmental Biology and Endocrine Research for a Successful Pregnancy*" was to bring together and highlight the original research and reviews on the recent advancements in the work for successful pregnancy. This Research Topic includes a diverse range of studies, including seven original research articles, six reviews, and two retrospective cohort studies.

A successful pregnancy concerns us all. Knowing the phases and disorders of female reproductive stages is crucial. Liu et al reviewed the role of oxytocin (OT) in the health and

disease of women. They explained how OT controls the reproductive cycle and pregnancy's physiological phases. OT helps GnRH release, ovulation, lactation, fetus expulsion, milk ejection, and maternal behavior. This review also discusses how OT affects maternal depression and hypogalactia. Endocrine-Disrupting Chemicals (EDCs) and physiological endocrine or hormonal systems are of concern today. EDCs originate from both natural sources, such as plants, and industrial/artificial sources. Pool et al. examined how phytoestrogens affect sheep reproduction. They discussed the way estrogenic pasture impairs sheep's reproduction. The relevance of estrogenic herbs on reproduction and pregnancy problems, including dystocia, stillborn lambs, and uterine prolapse after parturition (1–4), was stressed in their review. Endocrine disruptive substances' effects on specific *in-utero* development periods are poorly understood. If phytoestrogens breach the blood-placenta barrier and enter fetal tissue (5, 6), Pool et al. warn that estrogenic substances may affect gestational outcomes *in utero*. Although the long-term effect of *in-utero* exposure to phytoestrogens have not yet been established, neonatal exposure has been documented to cause precocious vaginal opening (7), ovarian follicle atresia (8), increased uterine fluid content (9), and hyperplasia of the endometrium (9–11) in rodents. Basak et al. also discussed that maternal endocrine balance is crucial for pregnancy. EDCs in daily life can impact pregnancy and outcomes if they exceed permissible concentrations, affecting implantation, placental development, fetal organ development, and epigenetics (12–16). Therefore, EDC awareness is crucial for reproduction, fertility, and pregnancy success. Basak et al. review the effects of EDCs, specifically bisphenols and phthalates, on fetoplacental growth and pregnancy outcomes.

Maternal obesity, gestational diabetes, preeclampsia, and cardiomyopathy are prominent pregnancy-related disorders. Exercise is safe and useful during pregnancy. Regular aerobic, anaerobic, and circular activities help pregnant humans and animals (17–19). Pahlavani reviewed the role of exercise in combating pregnancy complications, focusing on apelin in exercise-induced pregnancy problem protection. Pahlavani's review sheds light on the molecular mechanisms of exercise, including the ALPN/APJ system, which has been extensively studied across various body systems and species (20–25). Shokrollahi et al. found that buffalo ovarian follicles regulate the ALPN/APJ system, affecting buffalo fertility. They also highlighted the role of adipokines in endocrine control and steroidogenesis, suggesting that IGF1 or FSH-based involvement could aid in therapeutic ALPN/APJ system use.

The placenta and trophoblast are crucial for pregnancy establishment and maintenance, but abnormalities in the trophoblast and its protein and gene functions can lead to pregnancy termination. S100P is one of them, which was first purified and characterized from the placenta (26–28). Zhou et al. found that S100P positively regulates trophoblast syncytialization during the earlier stages of pregnancy establishment through the regulation of YAP1 protein and is present in many other tissues as well (29, 30). The results from Zhou et al. showed lower S100P as a poor pregnancy outcome marker for humans. Another peptide and

its receptor, kisspeptin, have an established role in reproduction as a whole (31–33). It is expressed in a wider range of tissue along with the placenta. Researchers depicted its role in pregnancy (34, 35). Tsoutsouki et al. have explored kisspeptin levels as potential pregnancy complication markers. They suggest kisspeptin levels could be useful in early pregnancy losses alongside beta-HCG measurement. Kisspeptin levels have been found to be variable during preeclampsia, suggesting a need for further study to ensure pregnancy health and success. In this Research Topic, Zhou et al. studied the role of VTCN1 at the human maternal-fetal interface. VTCN1 (B7-H4)'s expression in the first week's villous trophoblast was recently described (36). As VTCN1 has several functions and roles in immune homeostasis, its immunological involvement at the maternal-fetal interface could also be an important factor. Zhou et al. explained VTCN1 as an important regulator of trophoblast syncytialization and invasiveness during early placentation. Hence, VTCN1 could also be involved with abnormal placentation and diseases associated with abnormal placentation during pregnancy. The normal function of the placenta is also dependent on the ubiquitously expressed renin-angiotensin system (RAS) (37). The components of RAS, Angiotensin II (Ang II), and Angiotensin (1-7) (Ang-(1-7)) contributed to the normal physiological function of the reproductive processes such as follicular growth and development and the function of the placenta. Liu et al. summarize the localization and role of Ang II and Ang-(1-7) in the female reproductive system. A concreted understanding of the RAS and involvement of Ang II and Ang-(1-7) may aid in the understanding and maintenance of a healthy pregnancy. Whenever we consider the placental abnormalities, Kong et al., with a retrospective cohort study, found that IVF and maternal age are related to placental abnormalities. Extensive research is needed to determine if there is a connection between biological and molecular mechanisms causing placental pathological conditions in IVF and aged human pregnancies. Along with human studies, Bai et al. studied the insight into bovine pregnancy establishment and the role of the stromal protein PGE2 in bovines. Along with IFN tau, PGE2 from endometrial stromal cells helps maintain pregnancy with its luteoprotective function. Bai et al. demonstrated the molecular mechanism of how PGE2 helps in pregnancy maintenance. Bai et al. identified the PGE2-mediated factors viz. NFIL3 and CEBPA expression, might help in early-stage pregnancy establishment.

Polycystic ovary syndrome (PCOS) affects 6 to 15% of women of reproductive age (38). PCOS is also associated with miscarriage, gestational diabetes mellitus, hypertensive disorders of pregnancy, preterm delivery, and the birth of small-for-gestational-age (SGA) infants. Considering mRNA levels, Ren et al. stated that the PNA mouse is the best animal model for studying PCOS. Although a high percentage of women are affected by PCOS, its screening is not yet straightforward. Therefore, biomarkers could be of paramount importance here. Earlier studies highlighted that follicular microenvironments are related to PCOS (39). The pilot study by Ding et al., with the aim of searching for biomarkers of PCOS from follicular fluid, has successfully identified twenty-three lipid subclasses as potential biomarkers of PCOS in women. This study

could help in developing diagnostic markers and an accurate and early screen of PCOS in women.

SGA and large-for-gestational-age (LGA) infants are always at greater risk of obstetrical and gynecological complications (40, 41). Much research has been conducted with regard to the transportation functions of the placenta. Maternal lipid viz, total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c) are taken up by the placenta and actively participate in maternal-fetal metabolism and development (42, 43). In their retrospective study, Zhu et al. found that a higher lipid profile is associated with higher birth weight in the first trimester. They also found an increased risk of (LGA) and macrosomia. Although it is not routinely practiced, Zhu et al. show that measuring pregnant women's first trimester's lipid profile is advisable.

However, comparatively less research has been conducted on the placenta, an endocrine organ. Placental-secreted hormones and growth factors directly contribute to fetal development and pregnancy maintenance (44–49). Lopez-Tello; Sferruzzi-Perri explored the placental endocrine function and identified placental hormones as key fetal growth and pregnancy maintenance regulators. In conclusion, it could be stated that this Research Topic combined research articles that could help researchers and scientists generate ideas for a sound and healthy pregnancy outcome.

References

- Adams N. Pathological changes in the tissues of infertile ewes with clover disease. *J Comp Pathol.* (1976) 86:29–35. doi: 10.1016/0021-9975(76)90024-4
- Bennetts H, Underwood E, Shier FL. A specific breeding problem of sheep on subterranean clover pastures in Western Australia. *Veterinary J.* (1946) 102:348–52. doi: 10.1016/S0372-5545(17)31252-X
- Morley F, Axelsen A, Bennett D. Recovery of normal fertility after grazing on oestrogenic red clover. *Aust Veterinary J.* (1966) 42:204–6. doi: 10.1111/j.1751-0813.1966.tb04690.x
- George J. The incidence of dystocia in fine-wool merino ewes. *Aust Veterinary J.* (1975) 51:262–5. doi: 10.1111/j.1751-0813.1975.tb06931.x
- Doerge DR. Bioavailability of soy isoflavones through placental/lactational transfer and soy food. *Toxicol Appl Pharmacol.* (2011) 254:145–7. doi: 10.1016/j.taap.2010.10.018
- Doerge DR, Churchwell MI, Chang HC, Newbold RR, Delclos KB. Placental transfer of the soy isoflavone genistein following dietary and gavage administration to sprague dawley rats. *Reprod Toxicol.* (2001) 15:105–10. doi: 10.1016/S0890-6238(01)00108-3
- Murthy DRK, Reddy CM, Patil SB. Effect of benzene extract of hibiscus rosa sinensis on the estrous cycle and ovarian activity in albino mice. *Biol Pharm Bull.* (1997) 20:756–8. doi: 10.1248/bpb.20.756
- Awoniyi CA, Roberts D, Veeramachaneni DR, Hurst BS, Tucker KE, Schlaff WD. Reproductive sequelae in female rats after in utero and neonatal exposure to the phytoestrogen genistein. *Fertility Sterility.* (1998) 70:440–7. doi: 10.1016/S0015-0282(98)00185-X
- Tinwell H, Soames AR, Foster JR, Ashby J. Estradiol-type activity of coumestrol in mature and immature ovariectomized rat uterotrophic assays. *Environ Health Perspect.* (2000) 108:631–4. doi: 10.1289/ehp.00108631
- Baker V, Hepburn P, Kennedy S, Jones P, Lea L, Sumpter J, et al. Safety evaluation of phytosterol esters. Part 1. Assessment of oestrogenicity using a combination of in vivo and in vitro assays. *Food Chem Toxicol.* (1999) 37:13–22. doi: 10.1016/S0278-6915(98)00101-X
- Chen CY. Dietary genistein exerts estrogenic effects upon the uterus, mammary gland and the hypothalamic/pituitary axis in rats. *J Nutr.* (1997) 127:263–9. doi: 10.1093/jn/127.2.263
- Rolfo A, Nuzzo AM, De Amicis R, Moretti L, Bertoli S, Leone A. Fetal–maternal exposure to endocrine disruptors: correlation with diet intake and pregnancy outcomes. *Nutrients.* (2020) 12:1744. doi: 10.3390/nu12061744
- Basak S, Das MK, Duttaroy AK. Plastics derived endocrine-disrupting compounds and their effects on early development. *Birth Defects Res.* (2020) 112:1308–25. doi: 10.1002/bdr2.1741
- Gingrich J, Ticiani E, Veiga-Lopez A. Placenta disrupted: endocrine disrupting chemicals and pregnancy. *Trends Endocrinol Metab.* (2020) 31:508–24. doi: 10.1016/j.tem.2020.03.003
- Yang C, Song G, Lim W. A mechanism for the effect of endocrine disrupting chemicals on placentation. *Chemosphere.* (2019) 231:326–36. doi: 10.1016/j.chemosphere.2019.05.133
- Cariati F, D'Uonno N, Borrillo F, Iervolino S, Galdiero G, Tomaiuolo R. Bisphenol A: an emerging threat to male fertility. *Reprod Biol Endocrinol.* (2019) 17:1–8. doi: 10.1186/s12958-018-0447-6
- May LE, Allen JJ, Gustafson KM. Fetal and maternal cardiac responses to physical activity and exercise during pregnancy. *Early Hum Dev.* (2016) 94:49–52. doi: 10.1016/j.earlhumdev.2016.01.005
- May LE, Knowlton J, Hanson J, Suminski R, Paynter C, Fang X, et al. Effects of exercise during pregnancy on maternal heart rate and heart rate variability. *PM&R.* (2016) 8:611–7. doi: 10.1016/j.pmrj.2015.11.006
- May LE, Scholtz SA, Suminski R, Gustafson KM. Aerobic exercise during pregnancy influences infant heart rate variability at one month of age. *Early Hum Dev.* (2014) 90:33–8. doi: 10.1016/j.earlhumdev.2013.11.001
- Cheng J, Luo X, Huang Z, Chen L. Apelin/apj system: A potential therapeutic target for endothelial dysfunction-related diseases. *J Cell Physiol.* (2019) 234:12149–60. doi: 10.1002/jcp.27942
- Shimizu T, Kosaka N, Murayama C, Tetsuka M, Miyamoto A. Apelin and apj receptor expression in granulosa and theca cells during different stages of follicular development in the bovine ovary: involvement of apoptosis and hormonal regulation. *Anim Reprod Sci.* (2009) 116:28–37. doi: 10.1016/j.anireprosci.2009.01.009
- Shirasuna K, Shimizu T, Sayama K, Asahi T, Sasaki M, Berisha B, et al. Expression and localization of apelin and its receptor apj in the bovine corpus luteum during the estrous cycle and prostaglandin F2alpha-induced luteolysis. *Reproduction.* (2008) 135:519–25. doi: 10.1530/rep-07-0409
- Roche J, Ramé C, Reverchon M, Mellouk N, Cornuau M, Guerif F, et al. Apelin (Apln) and apelin receptor (Aplnr) in human ovary: expression, signaling, and regulation of steroidogenesis in primary human luteinized granulosa cells. *Biol Reprod.* (2016) 95:104. doi: 10.1095/biolreprod.116.141754

Author contributions

JB: Conceptualization, Writing – original draft, Writing – review & editing. AR: Writing – review & editing. BB: Writing – review & editing. KI: Writing – review & editing. LE: Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

24. Rak A, Drwal E, Rame C, Knapczyk-Stwora K, Słomczyńska M, Dupont J, et al. Expression of apelin and apelin receptor (Apj) in porcine ovarian follicles and in vitro effect of apelin on steroidogenesis and proliferation through apj activation and different signaling pathways. *Theriogenology*. (2017) 96:126–35. doi: 10.1016/j.theriogenology.2017.04.014
25. Roche J, Ramé C, Reverchon M, Mellouk N, Rak A, Froment P, et al. Apelin (Apln) regulates progesterone secretion and oocyte maturation in bovine ovarian cells. *Reproduction*. (2017) 153:589–603. doi: 10.1530/REP-16-0677
26. Becker T, Gerke V, Kube E, Weber K. S100p, a novel ca^{2+} -binding protein from human placenta: cDNA cloning, recombinant protein expression and ca^{2+} binding properties. *Eur J Biochem*. (1992) 207:541–7. doi: 10.1111/j.1432-1033.1992.tb17080.x
27. Donato R. S100: A multigenic family of calcium-modulated proteins of the e-hand type with intracellular and extracellular functional roles. *Int J Biochem Cell Biol*. (2001) 33:637–68. doi: 10.1016/S1357-2725(01)00046-2
28. De Clercq K, Pérez-García V, Van Bree R, Pollastro F, Peeraer K, Voets T, et al. Mapping the expression of transient receptor potential channels across murine placental development. *Cell Mol Life Sci*. (2021) 78:4993–5014. doi: 10.1007/s00018-021-03837-3
29. Permyakov SE, Denesyuk AI, Denessiouk KA, Permyakova ME, Kazakov AS, Ismailov RG, et al. Monomeric state of S100p protein: experimental and molecular dynamics study. *Cell Calcium*. (2019) 80:152–9. doi: 10.1016/j.ceca.2019.04.008
30. Tong X-M, Lin X-N, Song T, Liu L, Zhang S-Y. Calcium-binding protein S100p is highly expressed during the implantation window in human endometrium. *Fertility Sterility*. (2010) 94:1510–8. doi: 10.1016/j.fertnstert.2009.07.1667
31. Brahmer A, Neuberger EWI, Simon P, Krämer-Albers E-M. Considerations for the analysis of small extracellular vesicles in physical exercise. *Front Physiol*. (2020) 11:576150. doi: 10.3389/fphys.2020.576150
32. Seminara SB, Messenger S, Chatzidaki EE, Thresher RR, Acierno JS Jr., Shagoury JK, et al. The gpr54 gene as a regulator of puberty. *New Engl J Med*. (2003) 349:1614–27. doi: 10.1056/NEJMoa035322
33. Lee J-H, Miele ME, Hicks DJ, Phillips KK, Trent JM, Weissman BE, et al. Kiss-1, a novel human Malignant melanoma metastasis-suppressor gene. *JNCI: J Natl Cancer Institute*. (1996) 88:1731–7. doi: 10.1093/jnci/88.23.1731
34. Park DW, Lee SK, Hong SR, Han AR, Kwak-Kim J, Yang KM. Expression of kisspeptin and its receptor gpr54 in the first trimester trophoblast of women with recurrent pregnancy loss. *Am J Reprod Immunol*. (2012) 67:132–9. doi: 10.1111/j.1600-0897.2011.01073.x
35. Hu K-L, Chang H-M, Zhao H-C, Yu Y, Li R, Qiao J. Potential roles for the kisspeptin/kisspeptin receptor system in implantation and placentation. *Hum Reprod Update*. (2018) 25:326–43. doi: 10.1093/humupd/dmy046
36. Karvas RM, McInturf S, Zhou J, Ezashi T, Schust DJ, Roberts RM, et al. Use of a human embryonic stem cell model to discover gabrp, wfdc2, vtcn1 and actc1 as markers of early first trimester human trophoblast. *Mol Hum Reprod*. (2020) 26:425–40. doi: 10.1093/molehr/gaaa029
37. Herr D, Bekes I, Wulff C. Local renin-angiotensin system in the reproductive system. *Front Endocrinol*. (2013) 4:150. doi: 10.3389/fendo.2013.00150
38. Kamalanathan S, Sahoo JP, Sathyapalan T. Pregnancy in polycystic ovary syndrome. *Indian J Endocrinol Metab*. (2013) 17:37–43. doi: 10.4103/2230-8210.107830
39. Dai G, Lu G. Different protein expression patterns associated with polycystic ovary syndrome in human follicular fluid during controlled ovarian hyperstimulation. *Reproduction Fertility Dev*. (2012) 24:893–904. doi: 10.1071/RD11201
40. Sharma D, Shastri S, Sharma P. Intrauterine growth restriction: antenatal and postnatal aspects. *Clin Med Insights: Pediatr*. (2016) 10:67–83. doi: 10.4137/CMPed.S40070
41. Ng S-K, Olog A, Spinks AB, Cameron CM, Searle J, McClure RJ. Risk factors and obstetric complications of large for gestational age births with adjustments for community effects: results from a new cohort study. *BMC Public Health*. (2010) 10:1–10. doi: 10.1186/1471-2458-10-460
42. Brett KE, Ferraro ZM, Yockell-Lelievre J, Gruslin A, Adamo KB. Maternal–fetal nutrient transport in pregnancy pathologies: the role of the placenta. *Int J Mol Sci*. (2014) 15:16153–85. doi: 10.3390/ijms150916153
43. Barbour LA, Hernandez TL. Maternal lipids and fetal overgrowth: making fat from fat. *Clin Ther*. (2018) 40:1638–47. doi: 10.1016/j.clinthera.2018.08.007
44. Napso T, Yong HE, Lopez-Tello J, Sferruzzi-Perri AN. The role of placental hormones in mediating maternal adaptations to support pregnancy and lactation. *Front Physiol*. (2018) 9:387601. doi: 10.3389/fphys.2018.01091
45. Lopez-Tello J, Jimenez-Martinez MA, Salazar-Petres E, Patel R, George AL, Kay RG, et al. Identification of structural and molecular signatures mediating adaptive changes in the mouse kidney in response to pregnancy. *Int J Mol Sci*. (2022) 23:6287. doi: 10.3390/ijms23116287
46. Napso T, Zhao X, Lligoña MI, Sandovici I, Kay RG, George AL, et al. Placental secretome characterization identifies candidates for pregnancy complications. *Commun Biol*. (2021) 4:701. doi: 10.1038/s42003-021-02214-x
47. Freemark M. Placental hormones and the control of fetal growth. *J Clin Endocrinol Metab*. (2010) 95:2054–7. doi: 10.1210/jc.2010-0517
48. Murphy VE, Smith R, Giles WB, Clifton VL. Endocrine regulation of human fetal growth: the role of the mother, placenta, and fetus. *Endocrine Rev*. (2006) 27:141–69. doi: 10.1210/er.2005-0011
49. Handwerger S, Freemark M. The roles of placental growth hormone and placental lactogen in the regulation of human fetal growth and development. *J Pediatr Endocrinol Metab*. (2000) 13:343–56. doi: 10.1515/JPEM.2000.13.4.343