SYSTEMATIC REVIEW

How often is the placenta included in human pregnancy research? A rapid systematic review of the literature [version 1; peer review: 2 approved with reservations]

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Abstract

Background: The placenta is a complex organ that plays a vital role not only in nutrient transfer but also in directing maternal and fetal physiological processes across pregnancy. Due to its multi-functionality, assessing the placenta can provide critical information about maternal and child health and risks of adverse outcomes.
Objective: We aimed to quantify the percentage of human pregnancy studies that include placenta data.
Methods: We conducted a rapid review of pregnancy studies conducted in the US that were published as original research in PubMed in 2018. Human studies conducted during the second trimester, third trimester, or labor and/or delivery were eligible. The systematic search produced 1,448 publications. After screening and full article review, 290 studies met all eligibility criteria. We then extracted data on study design, reporting of placenta data, time and type of data collection, and study objective categorization.
Results: In total, 32% of studies were randomized controlled trials; the remaining were observational studies. Only 14% included placenta data of any kind. A total of 10% included placenta data during pregnancy and 7% included data after delivery; only 2% included both. Most data during pregnancy were collected by ultrasound and most data on the delivered placenta were from pathology exams. Study objectives were focused on maternal and/or infant outcomes (99.7%), while only one study had a placenta outcome.
Conclusion: Based on this rapid review, a small proportion of pregnancy studies use placenta data in research. The placenta, an essential component of understanding healthy or adverse outcomes, deserves much more attention in pregnancy research.

Keywords

pregnancy, placenta, rapid review, pathology, ultrasound

Open Peer Review

Approval Status ? ?

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Almudena Veiga-Lopez, University of Illinois-Chicago, Chicago, USA

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Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: Taylor LA: Conceptualization, Data Curation, Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Gallagher K**: Data Curation, Writing – Review & Editing; **Ott KA**: Data Curation, Writing – Review & Editing; **Gernand AD**: Conceptualization, Data Curation, Formal Analysis, Methodology, Project Administration, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing

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Introduction

It has long been known that the placenta is a complex organ with a vital role in all aspects of fetal growth and survival including gas exchange, nutrient transport, hormone synthesis and protection against pathogens[1,2]. Despite its immense importance, researchers have recognized it as the "least understood human organ"[3] and "multitalented, but still mysterious"[4]. These acknowledgements spurred the establishment of the Human Placenta Project by the National Institutes of Health in 2014 to increase research particularly relevant to in utero placental development[5].

A large body of research links complications of pregnancy, including preeclampsia, intrauterine growth restriction, and preterm birth to disorders of placentation, affirming the significance of placental health to the health of the pregnancy and fetus[6–8]. Furthermore, women with placental disease such as maternal vascular malperfusion are at higher risk of developing cardiovascular disease later in life[9,10]. The importance of the placenta in the health of the offspring is evidenced in connections between placental morphology (such as placental surface size, placental weight, and maternal cotyledons) and childhood hypertension[11], asthma[12], and disorders of eye development[13], as well as cardiovascular disease and obesity later in life[1]. The placenta's role in chronic disease outcomes has become central in the developmental origins of health and disease hypothesis[14].

While there is extensive research showing the associations between placental characteristics and a wide range of pregnancy disorders and maternal and child health outcomes, to our knowledge, the extent of all pregnancy research that incorporates data on the placenta has not been evaluated. The primary aim of this rapid review was to quantify the percentage of human pregnancy studies that include placenta data. We secondarily aimed to categorize and describe the placenta data being reported.

Methods

We conducted a rapid systematic review of published pregnancy studies, closely following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[15] but limiting the scope to be more rapid in nature: we searched one database (PubMed) for articles of research in the US published within a one-year period (2018). The search strategy for PubMed was the following:

"pregnancy"[MeSH] AND (Observational Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Randomized Controlled Trial[ptyp] OR Multicenter Study[ptyp] OR Comparative Study[ptyp] NOT Review[ptyp] NOT Meta-Analysis[ptyp] NOT Systematic Review[ptyp] NOT Case Reports[ptyp] NOT Letter[ptyp] NOT Comment[ptyp]) AND ("2018/01/01"[PPDAT] : "2018/12/31"[PPDAT]) AND "humans"[MeSH Terms] AND English[lang] NOT Africa[MeSH] NOT Asia[MeSH] NOT Central America[MeSH] NOT South America[MeSH] NOT Latin America[MeSH] NOT Caribbean Region[MeSH] NOT Europe[MeSH] NOT Islands[MeSH] NOT Oceania[MeSH] NOT Canada[MeSH]

The last search was completed on November 27, 2019. We did not register this rapid review in PROSPERO due to time constraints, and this review did not require ethical approval.

Inclusion criteria

Peer-reviewed, original human research focusing on pregnancy in the second trimester, third trimester, and/or labor and delivery were included in this search. Studies were eligible if published between January 1, 2018 and December 31, 2018, according to the publication date available in PubMed. Studies had to be conducted in the United States and published in English. If the study location was not specified in the publication, author affiliations were checked for locations and deemed eligible if all or most authors had affiliations in the United States.

Exclusion criteria

Case reports and review articles were excluded, as well as in vitro studies or animal models. Studies confined to periconception or the first trimester of pregnancy (up to 12 weeks gestation) were also excluded. Because there is limited ability to study the developing placenta in vivo in humans during this early gestational time, we did not want to overinflate the percentage of pregnancy studies that did not include the placenta.

Study selection

We used Rayyan (Qatar Computing Research Institute, Doha, Qatar) to manage articles and record decisions during the review process. Three independent researchers (LAT, KG, KAO) reviewed articles at both the abstract and full article review stages, applying inclusion and exclusion criteria at both stages. If disagreements arose, all reviewers discussed the issue and formed a resolution, consulting with a fourth investigator (ADG) as needed. We did not appraise the quality or assess risk of bias of individual studies because this was beyond the scope of this rapid review.

Data extraction and pregnancy characteristics

The same three reviewers extracted data from the publications and compared results. If disagreements arose, all reviewers discussed the issue and formed a resolution. The following information was extracted from the publications: first author's last name, journal title, study design (randomized controlled trial, cohort, case control, cross-sectional), inclusion of placenta data (yes/no), time of placenta data collection (during pregnancy or after delivery), method of data collection (i.e., ultrasound, MRI, pathology), type of placenta data reported (i.e., placenta weight, estimated placental volume, placental abruption, etc.), and study objective(s). To determine if placenta data was reported, the authors searched each article in its entirety for "placenta" and related terms. We looked for any indication that placenta data was collected and reported. Study objectives were categorized into four groups: outcomes related to mother, infant, placenta, or a combination of 2–3 outcomes. Extracted data was recorded in an Excel (Version 2008) spreadsheet, in which all counts and percentages were calculated.

Results

A total of 1,448 publications were identified in the PubMed search. After screening titles and abstracts, 363 publications underwent full article review, and 290 studies met all eligibility criteria (Figure 1). A total of 42 studies reported placenta data in some capacity.

Over half of the total studies included in this review were cohort designs, almost a third were randomized controlled trials, and less than 10% were case-control studies or cross-sectional studies (Table 1). The proportion of studies within each study design was similar for those with and without placenta data compared to total studies, but a higher percentage of studies with placenta data tended to be observational designs compared to those without placenta data. Sample sizes covered an extremely wide range from very small to tens of millions. The range was 8 to 57 million subjects for all studies, 10 to 57 million for studies with placenta data, and 8 to 42 million for studies without placenta data.

Across all studies, 47% had study objectives targeting one or more outcomes solely related to the mother; over a third had

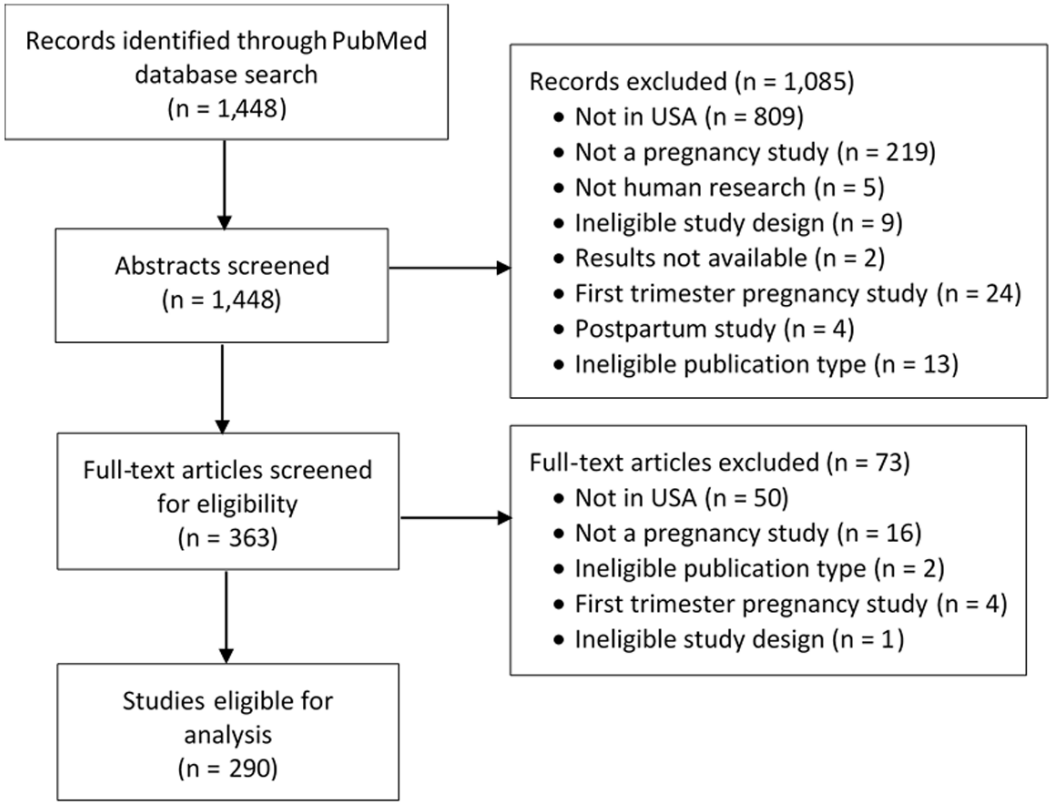

Figure 1. PRISMA flow diagram for study selection.

Table 1. Study designs of pregnancy studies conducted in the United States and published in 2018.

	All Studies (n=290)	With Placenta Data (n=42)	Without Placenta Data (n=248)
Study Design		**N (%)**	
Cohort study	170 (59)	28 (67)	142 (57)
Randomized controlled trial	94 (32)	9 (21)	85 (34)
Case-control study	18 (6)	3 (7)	15 (6)
Cross-sectional study	8 (3)	2 (5)	6 (2)

outcomes related solely to the infant, and 17% examine outcomes for both mother and infant (Figure 2). Only one study had a placenta outcome. Among the subset of 42 pregnancy studies that reported placenta data, over half were studies with infant outcomes. Finally, in the group of studies that did not report placenta data, the percentage of outcomes in each category was similar to the findings for all studies, with approximately half focused on maternal outcomes.

Of the studies with placenta data, 29 reported data collected during pregnancy, and 19 studies reported data collected after delivery (Figure 3). Five of these studies included placenta data from both pregnancy and postpartum. During pregnancy, 16 studies collected placenta data via ultrasound, 1 study collected placenta data via MRI, and 13 studies used other proxy methods for direct placenta measurements, such as clinical examinations and chart reviews (Table 2). After delivery, 13 studies collected placenta data via pathology examinations, and 8 studies collected placenta data via other methods (e.g., umbilical cord blood collected). Some data collection methods were unspecified (n=6).

Discussion

We conducted a systematic review to quantify the percentage of human pregnancy studies that include placenta data – limiting the scope to those conducted in the United States and published in 2018 to facilitate a rapid review. Fourteen percent of the studies reported placenta data, most of which was collected

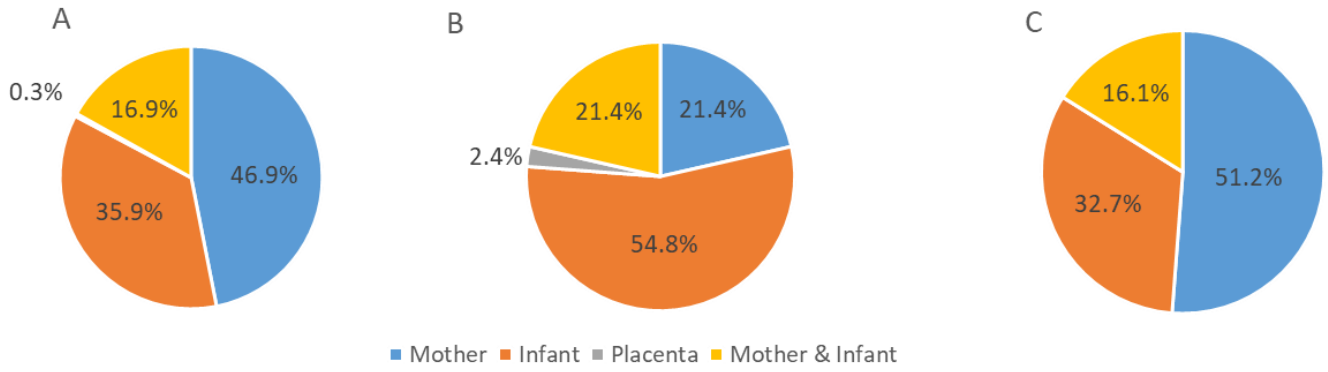

Figure 2. Categorization of study outcome(s) of human pregnancy studies conducted in the United States and published in 2018: (**A**) all studies (n=290); (**B**) studies that report placenta data (n=42); and (**C**) studies that do not report placenta data (n=248).

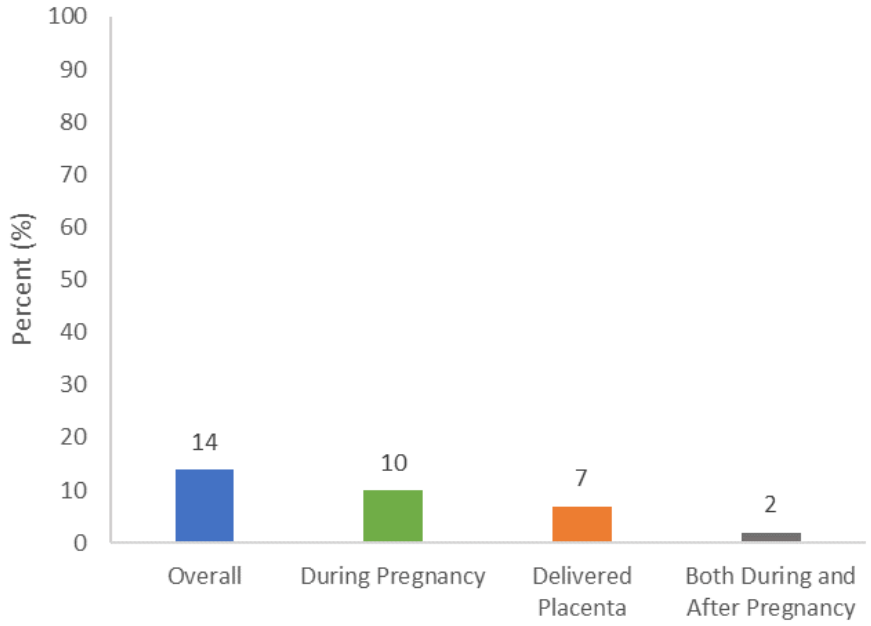

Figure 3. Percentage of pregnancy studies conducted in the United States and published in 2018 that report placenta data (n=290). Studies that report placenta data collection at both time points are counted more than once.

Table 2. Time and method of placenta data collection for human pregnancy studies conducted in the United States and published in 2018 that report placenta data (n=42).

Time and Method of Placenta Data Collection	N (%)[1]
During Pregnancy	29 (69)
Ultrasound	16 (38)
MRI	1 (2)
Other	13 (31)
Delivered Placenta	19 (45)
Pathology	13 (31)
Other	8 (19)

[1]Studies that report placenta data collection at both time points are counted more than once.

by ultrasound during pregnancy or through pathology exams after delivery. More studies that reported placenta data were focused on infant outcomes compared to studies without placenta data, which were focused more heavily on maternal outcomes. Only a single study, out of 290, focused on outcomes related directly to the placenta.

The placenta's invaluable role in pregnancy is undisputed - it dictates the success of growth and development in a pregnancy through a range of processes including nutrient sensing and endocrine signaling between mother and fetus. Abnormal placental development and dysfunction, along with fetal insults in utero, have been shown to impact the growth and development of offspring across the lifespan[14,16]. Assessing the placenta both during pregnancy and after delivery can shed light on the pathophysiology of adverse outcomes, including clues to early or late gestation insults. Scifres *et al.* found that in pregnant women with gestational diabetes mellitus, maternal vascular malperfusion lesions in the placenta were associated with excess gestational weight gain and lower infant birth weight, as well as increased risk of preterm birth and hypertensive disorders of pregnancy[17]. Similarly, Hauspurg *et al.* found that the presence of placental maternal vascular malperfusion in healthy pregnancies was associated with increased risk of adverse outcomes in later pregnancies[18]. In a cohort study of over 900 pregnant women, Salafia *et al.* found that placental disk size, including chorionic surface shape area and perimeter, was correlated with infant birth weight and gestational age at delivery[19].

However, assessing the placenta often requires extensive training, is time-consuming, and can quickly become expensive. Dimitrova *et al.* found that additional specialized training was needed to detect ultrasound indicators associated with placenta accreta spectrum disorders, compared to basic obstetric ultrasound training[20]. Some researchers have begun working to make placenta data collection easier, more common, and automated. Salafia and colleagues have used placenta images to examine variations in surface shape and vascular development, and how these can indicate the presence of maternal and fetal vascular pathologies[21]. Our group is working to develop rapid placenta assessment software based on photographs using artificial intelligence methods[22]. This and other work could help current and future pregnancy research to more easily include the placenta in pregnancy studies.

In our aim to assess the proportion of pregnancy research that utilizes the placenta, we chose to conduct a rapid systematic review as a first step toward this goal. Rapid reviews have become a helpful way to gather broad information and assess various topics, including those in healthcare. A rapid review can be conducted quickly, does not require multiple independent reviewers (although we did use multiple reviewers), and can provide broad descriptions and information of detailed topics[23]. Hummel *et al.* conducted a qualitative rapid review to evaluate ethical problems in healthcare for pregnant women in epidemics[24]. This review was able to quickly identify common healthcare-related risks and issues through a targeted database search, and qualitatively assess the proposed management plans for each. Antony *et al.* conducted a rapid review commissioned by the World Health Organization to evaluate the efficacy of quality improvement plans on patient safety in obstetrics[25]. Their review found that combined healthcare provider education and quality improvement plans could improve maternal and newborn safety during delivery. Most recently, researchers have conducted rapid reviews of Coronavirus Disease 2019 (COVID-19) during pregnancy to provide quick results during a rapidly spreading pandemic[26]. Our rapid review, similar to others, allowed us to examine a broad topic and a large number of studies without the constraints of traditional systematic reviews.

A major strength of our study was the rigorous systematic review process, guided by a PhD-level university librarian with expertise in health sciences literature. Additionally, this review was conducted by three reviewers, ensuring cross-checking of eligibility criteria and consistency in reviews. The main limitation of our work was the shorter time to complete the review. Due to this self-imposed constraint, we narrowed the scope of our review to include only one year of publications within a single database, which undoubtedly reduced the number of studies available for review. A drawback was that not all pregnancy studies provided detailed methods or gestational timing for the placenta data collection, limiting our ability to describe the studies in our assessment.

Conclusions

The placenta is not only of immense importance in each and every pregnancy, it is often the key to understanding short- and long-term outcomes for both mother and child. In this rapid review, we found that only a small proportion of pregnancy studies

report placenta data in research, and it is rare for human pregnancy studies in the US to focus on outcomes related directly to the placenta. Future systematic reviews could expand the publications years and locations of research or alternatively focus on methods papers to ascertain whether placenta data is being collected but not reported in analysis. Overall, this paper quantifies the low percentage of pregnancy studies that include the placenta and adds to the many publications highlighting the dearth of placenta research. Pregnancy researchers across all disciplines should aim to include the placenta in studies of maternal and infant outcomes.

Data availability

Underlying data

ScholarSphere (Penn State): Placenta Rapid Review Data Extraction_Scholarsphere for 'How often is the placenta included in human pregnancy research? A rapid systematic review of the literature', https://doi.org/10.26207/857e-0b73[27].

Reporting guidelines

ScholarSphere (Penn State): PRISMA checklist for 'How often is the placenta included in human pregnancy research? A rapid systematic review of the literature', https://doi.org/10.26207/0d78-9p53[28].

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We would like to acknowledge Dr. Christina Wissinger for her expert guidance in choosing the rapid review method and finalizing the search strategy. We would also like to acknowledge Celeste Beck for her overall support and guidance through the review process, as well as her assistance with using Rayyan for study selection.

References

1. Latendresse G, Founds S: **The Fascinating and Complex Role of the Placenta in Pregnancy and Fetal Well-being.** *J Midwifery Womens Health.* 2015; **60**(4): 360–70.
PubMed Abstract | Publisher Full Text

2. Myatt L, Thornburg KL: **Effects of Prenatal Nutrition and the Role of the Placenta in Health and Disease.** *Methods Mol Biol.* 2018; **1735**: 19–46.
PubMed Abstract | Publisher Full Text

3. Guttmacher AE, Maddox YT, Spong CY: **The Human Placenta Project: Placental structure, development, and function in real time.** *Placenta.* 2014; **35**(5): 303–4.
PubMed Abstract | Publisher Full Text | Free Full Text

4. Guttmacher AE, Spong CY: **The human placenta project: it's time for real time.** *Am J Obstet Gynecol.* 2015; **213**(4 Suppl): S3–5.
PubMed Abstract | Publisher Full Text

5. Sadovsky Y, Clifton VL, Burton GJ: **Invigorating placental research through the "Human Placenta Project".** *Placenta.* 2014; **35**(8): 527.
PubMed Abstract | Publisher Full Text

6. Fisher SJ: **Why is placentation abnormal in preeclampsia?** *Am J Obstet Gynecol.* 2015; **213**(4 Suppl): S115–22.
PubMed Abstract | Publisher Full Text | Free Full Text

7. Lyall F, Robson SC, Bulmer JN: **Spiral artery remodeling and trophoblast invasion in preeclampsia and fetal growth restriction: relationship to clinical outcome.** *Hypertension.* 2013; **62**(6): 1046–54.
PubMed Abstract | Publisher Full Text

8. Maltepe E, Fisher SJ: **Placenta: the forgotten organ.** *Annu Rev Cell Dev Biol.* 2015; **31**: 523–52.
PubMed Abstract | Publisher Full Text

9. Rana S, Lemoine E, Granger JP, *et al.*: **Preeclampsia: Pathophysiology, Challenges, and Perspectives.** *Circ Res.* 2019; **124**(7): 1094–112.
PubMed Abstract | Publisher Full Text

10. Crispi F, Miranda J, Gratacos E: **Long-term cardiovascular consequences of fetal growth restriction: biology, clinical implications, and opportunities for prevention of adult disease.** *Am J Obstet Gynecol.* 2018; **218**(2S): S869–S79.
PubMed Abstract | Publisher Full Text

11. Barker D, Osmond C, Grant S, *et al.*: **Maternal cotyledons at birth predict blood pressure in childhood.** *Placenta.* 2013; **34**(8): 672–5.
PubMed Abstract | Publisher Full Text | Free Full Text

12. Barker DJ, Osmond C, Forsen TJ, *et al.*: **Foetal and childhood growth and asthma in adult life.** *Acta Paediatr.* 2013; **102**(7): 732–8.
PubMed Abstract | Publisher Full Text

13. Lingham G, Mackey DA, Sanfilippo PG, *et al.*: **Influence of prenatal environment and birth parameters on amblyopia, strabismus, and anisometropia.** *J AAPOS.* 2020; **24**(2): 74.e1–74.e7.
PubMed Abstract | Publisher Full Text

14. Thornburg KL, Marshall N: **The placenta is the center of the chronic disease universe.** *Am J Obstet Gynecol.* 2015; **213**(4 Suppl): S14–20.
PubMed Abstract | Publisher Full Text | Free Full Text

15. Liberati A, Altman DG, Tetzlaff J, *et al.*: **The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration.** *PLoS Med.* 2009; **6**(7): e1000100.
PubMed Abstract | Publisher Full Text | Free Full Text

16. Barker DJ, Thornburg KL: **Placental programming of chronic diseases, cancer and lifespan: a review.** *Placenta.* 2013; **34**(10): 841–5.
PubMed Abstract | Publisher Full Text

17. Scifres CM, Parks WT, Feghali M, *et al.*: **Placental maternal vascular malperfusion and adverse pregnancy outcomes in gestational diabetes mellitus.** *Placenta.* 2017; **49**: 10–5.
PubMed Abstract | Publisher Full Text

18. Hauspurg A, Redman EK, Assibey-Mensah V, *et al.*: **Placental findings in non-hypertensive term pregnancies and association with future adverse pregnancy outcomes: a cohort study.** *Placenta.* 2018; **74**: 14–9.
PubMed Abstract | Publisher Full Text

19. Salafia CM, Shah RG, Misra DP, *et al.*: **Chorionic vascular "fit" in the human placenta: Relationship to fetoplacental outcomes.** *Placenta.* 2017; **59**: 13–8.
PubMed Abstract | Publisher Full Text | Free Full Text

20. Dimitrova I, Jauniaux E, Zosmer N, *et al.*: **Development of a training program for the ultrasound screening of placenta accreta spectrum disorders.** *Int J Gynaecol Obstet.* 2019; **147**(1): 73–7.
PubMed Abstract | Publisher Full Text

21. Salafia CM, Yampolsky M, Misra DP, *et al.*: **Placental surface shape, function, and effects of maternal and fetal vascular pathology.** *Placenta.* 2010; **31**(11): 958–62.
PubMed Abstract | Publisher Full Text | Free Full Text

22. Chen Y, Zhang Z, Wu C, *et al.*: **AI-PLAX: AI-based placental assessment and examination using photos.** *Comput Med Imaging Graph.* 2020; **84**: 101744.
PubMed Abstract | Publisher Full Text | Free Full Text

23. Tricco AC, Antony J, Zarin W, *et al.*: **A scoping review of rapid review methods.** *BMC Med.* 2015; **13**: 224.
PubMed Abstract | Publisher Full Text | Free Full Text

24. Hummel P, Saxena A, Klingler C: **Rapid qualitative review of ethical issues surrounding healthcare for pregnant women or women of reproductive age in epidemic outbreaks.** *Epidemiol Health.* 2018; **40**: e2018003.
PubMed Abstract | Publisher Full Text | Free Full Text

25. Antony J, Zarin W, Pham B, *et al.*: **Patient safety initiatives in obstetrics: a rapid review.** *BMJ Open.* 2018; **8**(7): e020170.
PubMed Abstract | Publisher Full Text | Free Full Text

26. Mullins E, Evans D, Viner RM, *et al.*: **Coronavirus in pregnancy and delivery: rapid review.** *Ultrasound Obstet Gynecol.* 2020; **55**(5): 586–92.
PubMed Abstract | Publisher Full Text

27. Taylor L, Gallagher K, Ott KA, *et al.*: **How often is the placenta included in human pregnancy research? A rapid systematic review of the literature.** ScholarSphere. Dataset. 2021.
http://www.doi.org/10.26207/857e-0b73

28. Taylor L, Gallagher K, Ott K, *et al.*: **PRISMA checklist for 'How often is the placenta included in human pregnancy research? A rapid systematic review of the literature.** ScholarSphere. Dataset. 2021.
http://www.doi.org/10.26207/0d78-9p53

Open Peer Review

Current Peer Review Status: ? ?

Version 1

Reviewer Report 07 September 2021

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I am overall very supportive of the concept of the analysis presented. It is important to look at research and consider our biases. In particular reproductive research is fraught with social, moral and ethical contradictions. But this analysis has many biases that were not well justified.

Why limit to just the USA? Why not compare if this is a systemic global problem of undervaluing placental research? Or if focused on the USA why not consider state-level variations?

Why just the placenta? Other reproductive organs could be considered such as the uterus and ovaries.

Why only one year? Why not perform a multi-year analysis to determine trends over time?

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Partly

Are the conclusions drawn adequately supported by the results presented in the review?
Partly

Competing Interests: We are conducting a similar analysis but on a broader aspect of

reproductive biology.

Reviewer Expertise: Bioinformatics, computational biology, pregnancy, placental biology and development, preeclampsia, genetics

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Reviewer Report 25 March 2021

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This mini-review undertakes a review of pregnancy studies conducted in the US that were published as original research in PubMed in 2018. Considering the critical role placenta plays in providing fetal support and placental dysfunctions contribute not only to pregnancy complications but to developmental origin of pathologies in the offspring, the topic focus of this review is timely. The time limitation the authors refer to for restricting the review of studies to 2018 is not well justified. The mini-review is well written, reader-friendly and gets across the message emphasizing the need for future investigations in this area .

The major study limitations are 1) the inclusion of only one year of publications within a single database that reduced the number of studies available for review and 2) a lack of a comprehensive evaluation of placental phenotypes (the authors indicate this is due to inadequate methodological details and missing information regarding timing of placental collection from the studies evaluated). Expanding the focus to include studies from at least 2019 would be more impactful.

At a minimum the authors need to include:

1. A table listing the placental outcomes that the placental studies considered in this review focused on.

2. A section providing recommendations as to what needs done to improve study focus on the placenta within human pregnancy research.

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Yes

Are the conclusions drawn adequately supported by the results presented in the review?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Developmental origin of diseases

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.