

BRAIN DEATH IN PREGNANCY: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Brain death is a rare event in pregnancy. A recent case series estimated the prevalence of pregnancy among brain dead patients at 2.5%. The care of a brain-dead pregnant women focuses on optimizing maternal recovery, considering fetal health impacts, and interventions for maternal support, including medication, radiation exposure, and preterm labor risks.

The aim: This study aims to investigate brain death in pregnancy.

Methods: By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and ScienceDirect, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

Results: In the PubMed database, the results of our search brought up 17 articles, whereas the results of our search on ScienceDirect brought up 11 articles. The results of the search conducted by title screening yielded a total 12 articles for PubMed and 6 articles for ScienceDirect. We compiled a total of 12 papers, 7 of which came from PubMed and 5 of which came from ScienceDirect. We excluded 2 review articles, 3 duplicate articles, 1 article having ineligible subject, and 1 discussion article. In the end, we included five research that met the criteria.

Conclusion: In this review, 80% of neonates were born alive. Somatic support of the brain-dead pregnant woman was performed to maximize perinatal outcomes. And during gestation, obstetricians must closely monitored fetal development.

Keywords: brain death, pregnancy, delivery, gestational age, perinatal

INTRODUCTION

Brain death (BD) indicates an irreversible loss due to the failure in the whole brain and brain stem functions and physiopathologically intracranial circulation.¹ The Australian and New Zealand Intensive Care Society explains that BD is distinguished by irreversible unresponsive coma, and an combined with absence of brain-stem reflexes and respiratory center function. Further, for BD to be diagnosed, clinical or neuro-imaging evidence of acute brain pathology must be demonstrated which is consistent with irreversible neurological functional loss.²

Seifi, et al. (2020), BD was reported in 0.039% of the total hospital discharges and 2.063% of all deaths in the United States. However, the incidence of BD diagnosis increased significantly and gradually year to year. The increase in the diagnostic incidence of BD was mainly observed in hospitalized patients in large, urban hospitals with some integrated teaching systems.³

Two of three concepts of brain death/death by neurologic criteria (BD/ DNC) exist as the dominant accepted understanding of the term. The first and most widely accepted is the "whole brain" formulation which asserts that brain death is equivalent to catastrophic injury to all the major structures of the brain including the hemispheres, diencephalon, brainstem, and cerebellum. In this view, confirmation of complete and permanent damage to the whole brain should be confirmed before BD/DNC is ultimately declared.⁴ The diagnosis of BD, in general, is made in intensive care unit (ICU) and is based on the exhaustive clinical neurological examination, certified by a series of complementary studies that, depending on the country, may be mandatory.³

Disorders of consciousness and brain death are rare events in pregnancy.⁵ The incidence of brain death in pregnant women in the UK is unknown; such data are not routinely collected by intensive care units, or NHS Blood and Transplant (NHSBT). A recent case series estimated the prevalence of pregnancy among brain dead patients at 2.5%.⁶

Organ failure is an important cause of morbidity and mortality in the world. The most frequently encountered organ failure could be listed as kidney, heart, liver, and hematologic system failures. Therefore, BD diagnosis and maintaining good donor care gain more importance for patients waiting for organ transplantation.¹ Decisions regarding care of the pregnant patient will center on optimizing chances for maternal recovery, while taking stock of the impact the insult may have had on fetal health, and the effects on the fetus of the interventions required for maternal support (i.e., impact of ongoing medication and radiation exposure on fetal development, risk of maternal infections, and risks of preterm labor and delivery at extreme prematurity).⁵ This study aims to investigate brain death in pregnancy.

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this systematic review, we investigate brain death in women with pregnancy. It is possible to accomplish this by researching or investigating brain death in pregnancy, gestational age, and delivery. In addition, we also investigate neonatal outcomes. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine the incidence of brain death in pregnancy, gestational age, delivery, and neonatal outcomes. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published within the last 10 years. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "brain death"; "brain dead"; "pregnancy"; and "outcomes" as keywords. The search for studies to be included in the systematic review was carried out from December, 08th 2023 using the PubMed and ScienceDirect databases by inputting the words: "brain death"[Title/Abstract] OR "brain dead"[Title/Abstract] AND "pregnancy"[MeSH Terms] OR "pregnancy"[All Fields] OR "pregnancies"[All Fields] OR "pregnancy s"[All Fields] AND "outcome"[All Fields] OR "outcomes"[All Fields] AND (y_10[Filter]) AND (english[Filter]) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

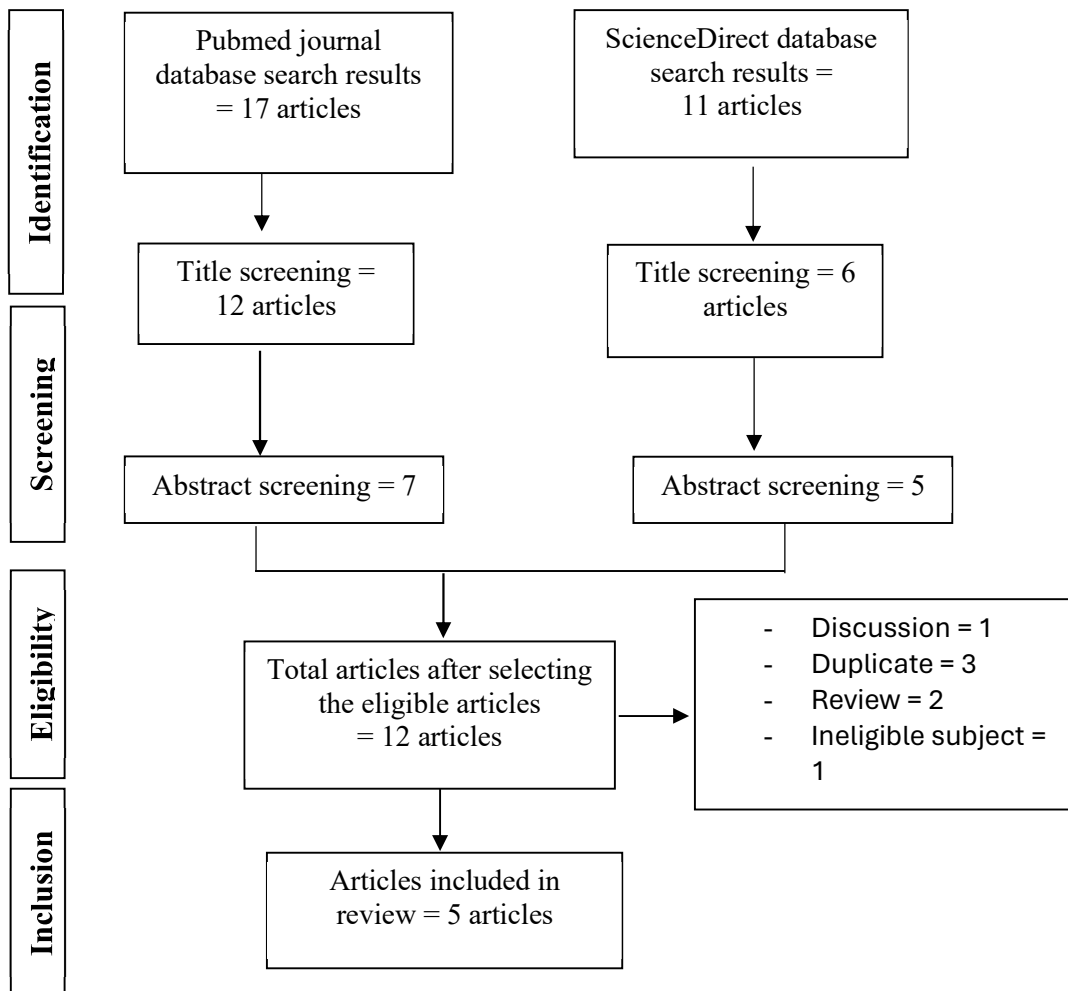


Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 17 articles, whereas the results of our search on ScienceDirect brought up 11 articles. The results of the search conducted by title screening yielded a total 12 articles for PubMed and 6 articles for ScienceDirect. We compiled a total of 12 papers, 7 of which came from PubMed and 5 of which came from

ScienceDirect. We excluded 2 review articles, 3 duplicate articles, 1 article having ineligible subject, and 1 discussion article. In the end, we included five research that met the criteria.

The causes of BD reported in this systematic review are AVM rupture, intracranial hemorrhage, cardiac arrest secondary to respiratory failure due to acute asthma exacerbation, cardiac arrest after hanging herself, and severe head injuries after a traffic accident. Four study reported that patients diagnosed with BD in their 2nd trimester, and one study in 1st trimester of pregnancy. One study reported that patient had a spontaneous abortion, while four study reported successful delivery (2 with cesarean delivery and 2 with vaginal delivery).

Gal, et al. (2021)⁷ reported a 27-year-old woman, diagnosed with BD in 2nd trimester of pregnancy. On gestation week 35, a healthy female infant was delivered via post-mortem cesarean section, with a birth weight of 2140 g and an Apgar score of 10/10/10 at 1, 5, and 10 minutes, respectively. During the entire ICU stay, standard monitoring of vital signs and laboratory testing was performed. Somatic support of the brain-dead woman was continued with the aim of reaching at least 32 weeks of pregnancy and delivering a viable fetus. The main goal of the somatic support was to provide a sufficient oxygen supply to all maternal organs, including the placenta. To accelerate fetal lung maturity, we administered betamethasone on HD 53 (gestation week 25) and on HD 86 (gestation week 30). The development of the fetus was monitored regularly by an obstetrician. Ultrasound examination with biometry of the fetus was performed weekly to assess the growth of the fetus and rule out any organ development malformation. Basal stimulation of the fetus was also performed. On HD 117 (gestation week 35), a female infant was delivered via post-mortem cesarean section. The newborn was admitted to the neonatal department and discharged after 11 days of uncomplicated hospitalization. Her weight at discharge was 2220 g. The baby was examined by a neurologist at 4 weeks, and 4, 9, and 12 months. Her neurologic status and psychomotor development were found to be in normal ranges.

Gopcevic, et al. (2017)⁸ reported a 34-year-old woman, diagnosed with BD in 2nd trimester of pregnancy. A conservative approach was adopted. The somatic support was performed until the patient reached 32 weeks of gestation and for cesarean delivery (CD) to be performed. No special interventions apart from regular fetal cardiotocography (CTG), biophysical profile monitoring and betamethasone therapy were needed during the pregnancy. At 29+2 weeks of gestation, fetal tachycardia with a basal frequency of 165 beats/min and unreactive undulatory oscillations were noted. An urgent CD was performed and a girl was delivered, weighing 1030g, with an Apgar score of 8/9 at 1 and 5 minutes, respectively. The neonate was admitted to the neonatal ICU and was discharged home 54 days later, following an uncomplicated post-delivery recovery.

Kang, et al. (2023)⁹ reported a 34-year-old pregnant female, diagnosed with BD in 2nd trimester of pregnancy. At the time of admission, live intrauterine gestational age (GA) with fetal heart rate of 129 BPM. The family requested to continue life support until viability of the fetus in order to attempt a live birth. But after 21 days of life support, the patient had a spontaneous abortion.

Kinoshita, et al. (2015)¹⁰ reported a 32-year-old pregnant female, diagnosed with BD in 2nd trimester of pregnancy. An informed decision was made to continue medical support. Obstetricians regularly checked the condition of the fetus. On the 92nd hospital day (at 33 weeks and 3 days of gestation) natural labor started without the use of any labor accelerator, and a healthy 2,130-g girl was delivered vaginally with minimum assistance by obstetricians. The baby's Apgar score was 6/8, and she was discharged 40 days after birth.

Reinhold, et al. (2019)¹¹ reported a 28-year-old woman, diagnosed with BD in 1st trimester of pregnancy. During gestation, primary focus was the preservation of homeostasis and organ function, in order to provide best available medical care for the fetus. Throughout gestation, obstetricians closely monitored fetal development. At 30+4 weeks, an assisted vaginal birth of a female child was performed. The child presented with an APGAR score of 7, 8 and 9 after 1, 5 and 10min, respectively. The preterm required a short period of ventilatory support due to respiratory distress but further course was uneventful. Seven weeks later, the age-appropriate developed girl was discharged from hospital.

Table 1. The literature include in this study

Author	Origin	Method	Gestational age at BD	Result
Gal, 2021 ⁷	Czechia, Europe	Case Report	16th week	A 27-year-old woman, secundigravida, had the successful delivery of a healthy child after 117 days of maternal somatic support, with overall good 1-year outcomes for the child.
Gopcevic, 2017 ⁸	Croatia, Europe	Case Report	20th week	A 34-year-old woman, secundigravida, an urgent CD was performed at 29+2 weeks of gestation and a girl was delivered, weighing 1030g, with an Apgar score of 8 and 9 at 1 and 5 minutes, respectively. The neonate was admitted to the neonatal ICU and was discharged home 54 days later, following an uncomplicated post-delivery recovery. Three years later the child was healthy, with normal neurological development and no somatic disease.
Kang, 2023 ⁹	USA	Case Report	15th week	A 34-year-old pregnant female at 15th week of gestation had a spontaneous abortion after 21 days of life support.
Kinoshita, 2015 ¹⁰	Japan	Case Report	20th week	A 32-year-old pregnant woman became brain dead on the 13th hospital day. On the 92nd hospital day at gestational week 33 + 3 days, natural labor began and a healthy 2,130-g girl (Apgar 6/8) was delivered vaginally with minimum assistance.

Reinhold,2019 ¹¹	Germany, Europe	Case Report	9th week	A 28-year-old had brain dead on day 8 after admission. At 30+4 weeks of gestation, a viable girl was born via assisted vaginal delivery.
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DISCUSSION

The purpose of this research was to review studies published after January of 2013 and up to December of 2023 that investigated the brain death in pregnancy. The causes of BD reported in this systematic review are AVM rupture, intracranial hemorrhage, cardiac arrest secondary to respiratory failure due to acute asthma exacerbation, cardiac arrest after hanging herself, and severe head injuries after a traffic accident.

Brain-dead patients experience a multitude of physiological insults resulting in a loss of essential homeostatic brain functions.⁶ In *PP v Health Service Executive* (hereafter ‘PP’), the Irish High Court was recently asked to decide on the lawfulness of maintaining somatic treatment that was being provided to a brain-dead woman who was 15-weeks pregnant.¹² Pregnancy is possibly the only condition in which somatic support may be considered to continue support for the sake of the fetus. As a result, if somatic support is being explored as a possibility, counselling needs to contain some information on prognosis. Age of the patient has an inverse relationship with survival capacity, and main brain illness is linked to longer survival than multisystem aetiologies.^{13,14}

In this review, four study reported that patients diagnosed with BD in their 2nd trimester, and one study in 1st trimester of pregnancy. BD patients undergo corporeal support to maintain death suspension until fetal health crises necessitate fetal excision via post mortem CS. Some studies report organ removal for transplantation, allowing 'final' death to occur, highlighting the delicate concept of death and fetal personhood. Despite the original intent of short-term use of corporeal support for organ transplatation purposes, a BD body has been corporeally supported for 107 days or 15.2 weeks solely for fetal benefit, construing prolonged corporeal support as a new reproductive technology, because it the aim is attainment of a live infant from the body of a long-dead woman. Sophisticated critical and neonatal intensive care and practices dovetail into this as these infants are often very ill and extremely premature and require prolonged intensive care. This is relevant because 14 years prior to the 2012 release of the International Federation of Gynecologists and Obstetricians’ (FIGO) statement that ‘no mandatory lower gestational age limit should be set for the onset of fetal rescue after maternal BD.’²

In this review, all of the babies were born preterm. Four study reported successful delivery (2 with cesarean delivery and 2 with vaginal delivery). Howeverm, one study reported that patient had a spontaneous abortion. Preterm birth is generally defined as one that occurs after 20 weeks of gestation and prior to 37 completed menstrual weeks of gestation. Viability refers to the lower limit of gestational age when newborn survival is possible after delivery. It is known that as gestational age at delivery decreases, neonatal morbidity and mortality rates increase and complica- tions of prematurity account for more infant deaths than any other cause. Surviving infants have increased risks of impairment in vision and hearing, chronic lung disease, cerebral palsy, and childhood developmental disorders. Given the real threat that prematurity places on a child’s health, the gestational age at the time of maternal injury and delivery are significant factors to consider if continuing life-sustaining treatment for purposes of reaching viability is planned.⁵

Fetal growth is influenced by the state of the BD body during pregnancy, with the first 12 weeks being particularly sensitive. Destabilization of the BD body can lead to complications such as placental insufficiency, oligohydramnios, fetal growth restriction, and distress. These infants often require post-mortem CS, ventilatory support, and intensive care. Long-term health implications are also emerging for infants delivered by CS prior to labor commencement.² In this review, ultrasound examination, fetal cardiotocography (CTG), biophysical profile monitoring were performed and betamethasone therapy was given during the pregnancy.

CONCLUSION

In this review, 80% of neonates were born alive. Somatic support of the brain-dead pregnant woman was performed to maximize perinatal outcomes. And during gestation, obstetricians must closely monitored fetal development.

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