Perinatal outcomes in pregnant women with hypertensive syndromes: An integrative review

Desfechos perinatais em gestantes com síndromes hipertensivas: Uma revisão integrativa

Desenlaces perinatales en mujeres embarazadas con síndromes hipertensivos: repaso integrador

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Abstract: Objective: To identify in the literature the perinatal outcomes in pregnant women with hypertensive syndromes. Method: It is an integrative review with a collection of publications indexed in LILACS, PUBMED, SCOPUS and WEB OF SCIENCE, during January 2017. The descriptors used were: pregnancy-induced hypertension, perinatal and neonatology care. Results: The perinatal outcomes with the highest incidence were: perinatal mortality, prematurity, low APGAR in the 1st and 5th minute of life, newborns small for gestational age, admission to the intensive care unit, intrauterine growth restriction, and cesarean delivery. Among the investigated pathologies, pre-eclampsia stood out (80.6%) and 3% of the articles addressed severe pre-eclampsia. Conclusions: Investigations that analyze the exposure of the fetus/neonate to the maternal condition of severe pre-eclampsia and chronic hypertension overlapped by pre-eclampsia, constitute knowledge gaps. Descriptors: Pregnancy-induced Hypertension; Perinatal care; Neonatology; Nursing; Review

Resumo: Objetivo: Identificar na literatura os desfechos perinatais em gestantes com síndromes hipertensivas. Método: Trata-se de uma revisão integrativa com coleta de publicações indexadas na LILACS, PUBMED, SCOPUS e WEB OF SCIENCE, durante janeiro de 2017. Os descritores utilizados foram: hipertensão induzida pela gravidez, assistência perinatal e neonatologia. Resultados: Os desfechos perinatais de maior incidência foram:

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mortalidade perinatal, prematuridade, baixo APGAR no 1º e 5º minuto de vida, recém-nascidos pequenos para idade gestacional, admissão na unidade intensiva, restrição de crescimento intraútero e parto cesariano. Dentre as patologias investigadas, destacou-se a pré-eclampsia (80,6%) e 3% dos artigos abordaram a pré-eclampsia grave. 

Conclusões: A realização de investigações que analisem a exposição do feto/neonato à condição materna da pré-eclampsia grave e da hipertensão crónica sobreposta por pré-eclampsia, constitui-se como gaps de conhecimento. 

Descritores: Hipertensão induzida pela gravidez; Assistência perinatal; Neonatologia; Enfermagem; Revisão

Resumen: Objetivo: Identificar en la literatura las conclusiones perinatales en mujeres embarazadas con síndromes hipertensivos. Método: se trata de un repaso integrador con recogida de publicaciones en la LILACS, PUBMED, SCOPUS e WEB OF SCIENCE, mientras enero de 2017. Los descriptores utilizados fueron: hipertensión inducida por el embarazo, atención perinatal y neonatología. Resultados: Las conclusiones perinatales de mayor incidencia han sido: mortalidad perinatal, prematuridad, bajo APGAR en el primer y quinto minuto de vida, recién nacidos pequeños para la edad gestacional, admisión en la unidad intensiva, restricción de crecimiento intrauterino y parto por cesárea. Entre las patologías investigadas, sobresalió la preeclampsia (80,6%) y 3% de los artículos han abordado la preeclampsia severa. Conclusiones: la realización de investigaciones que analicen la exposición del feto/neonato a la condición materna de la preeclampsia severa e hipertensión crónica solapamiento por preeclampsia se constituye como lagunas de conocimiento. 

Descritores: Hipertensión Inducida en el Embarazo; Atención Perinatal; Neonatología; Enfermería; Revisión

Introduction

According to the guidelines of the American College of Obstetricians and Gynecologists (ACOG), Hypertensive Syndromes in Pregnancy (HSP) are classified according to the time of onset, between the 20th week of gestation and the 12th week of postpartum, in addition to the presence of proteinuria and signs of severity. Based on this, their typologies are divided into Chronic Arterial Hypertension (CAH), Chronic Hypertension with Overlapping Pre-eclampsia (CHOPE), Isolated Pre-eclampsia (PE), Pre-eclampsia with signs of severity (PES) and eclampsia.¹

Hypertension during pregnancy is the leading cause of maternal mortality in the world, occurring in 6 to 17% of nulliparous pregnant women and 2 to 4% of multiparous women, of which 20 to 50% progress to PE.² In Brazil, in 2014, maternal mortality from HSP was represented by the coefficient of 10.8 deaths per 100,000 births.³ In parallel to maternal mortality data, the rate of early neonatal mortality from preventable causes, including cases related to hypertension during pregnancy, was 2.7 deaths for a proportion of 100,000 live births in 2014.⁴ It is observed that prematurity stands out as one of the main causes of neonatal deaths,⁵ these outcomes being recurrent
in the cases of women who develop HSP.⁶

A study carried out with pregnant women who were diagnosed with hypertensive syndromes had a high risk of having a newborn (NB) with an APGAR index below seven in the first (RR = 2.33, p < 0.001) and the fifth minute (RR = 2.96, p = 0.003), characterized as fetal hypoxia; in addition to a higher relative risk for prematurity (RR = 2.06, p = 0.017), low birth weight (RR = 2.33, p = 0.009), fetal death (RR = 2.36, p = 0.03) and delivery cesarean section with unfavorable outcome (RR = 4.41, p < 0.001).⁷

The data presented draws attention as a public health problem, mainly because they are preventable complications through adequate care during prenatal and childbirth, with health promotion actions aimed at the prevention of HSP, early detection and monitoring of maternal-fetal health. The knowledge and discussion of the research carried out on the theme, especially regarding the identification of elements such as country of origin, design, level of evidence produced and the investigated perinatal outcomes, becomes relevant to deepen the theoretical basis on the subject and to contribute to the identification of knowledge gaps. With this, it becomes possible to instigate the elaboration of new studies that fill the existing gaps to produce evidence that subsidizes clinical decision-making and that contributes to the advancement of science.

That said, the study aims to identify in the literature the perinatal outcomes in pregnant women with hypertensive syndromes.

**Method**

It is an integrative review, based on the synthesis and analysis of the results of published scientific research, which follows the following construction steps: elaboration of the integrative review protocol; data collection with inclusion of publications that brought relevant contributions and answers to the research question; extraction of the information contained in the study; analysis
and interpretation of data; and, finally, presentation and discussion of the review.8

To elaborate the guiding question, the PICO strategy was used, as recommended by the Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA): Patient: pregnant women with hypertensive syndromes; Intervention: not applicable; Comparison: not applicable; and Outcomes: perinatal outcomes. With the question of review: what are the perinatal outcomes in pregnant women with hypertensive syndromes evidenced in the literature?

Scientific publications indexed in the respective databases were investigated: LILACS, PUBMED, SCOPUS and WEB OF SCIENCE. Each database was accessed by two researchers simultaneously, on different computers, to guarantee the reliability of the study and collect the largest number of relevant articles. No search filters were added such as year of publication, country or magazine.

The collection was carried out in January 2017, using descriptors selected from Health Sciences Descriptors (HSD) and Medical Subject Headings (MESH): 1# Pregnancy-Induced Hypertension; 2# Perinatal Care; 3# Neonatology. The crossings used in the uncontrolled search were: (1 # AND 2 #); (1 # AND 3 #) and (1 # AND 2 # AND 3 #). The complete articles available in the selected databases were included; articles that show perinatal outcomes in pregnant women with hypertensive syndromes. Publications in the format of editorials, letters to the editor, abstracts, expert opinion, reviews, book chapters, theses, and dissertations or that did not address the research topic were excluded.

Regarding the definition of the level of evidence of the study, the classification of level of scientific evidence was used,9 which establishes the following classification: level I (evidence from systematic reviews or meta-analysis of relevant clinical trials); level II (evidence derived from at least one well-designed randomized controlled clinical trial); level III (well-designed clinical trials without randomization); level IV (well-designed cohort and case-control studies); level V (systematic review of descriptive and qualitative studies); level VI (evidence derived from...
a single descriptive or qualitative study); and level VII (opinion of authorities or report of expert committees). According to the same classification, levels I and II are considered strong evidence; levels III and V as moderate and levels VI and VII are seen as weak evidence.

The selection of publications was initiated by reading the titles and abstracts. Subsequently, studies that were not available in full, duplicated and those that had insufficient data to answer the research question were removed, resulting in a total of 31 publications. Figure 1 shows a flowchart for the selection of articles.

**Figure 1:** Flowchart of article selection based on the steps of identification, screening, eligibility and inclusion. Natal, Rio Grande do Norte, 2017.

Source: Data collected by the author.
Results

The characterization of the articles regarding the variables: magazine and year of publication, author, title and perinatal outcomes identified in the studies, are presented in Table 1. The publications started in 1998 and continued until 2016, with an average production of two articles per year. As for the language, one was written in Chinese, two in Portuguese and the others in English. Of the studies, four were multicentric and the rest had the following countries of origin: Brazil, United States, China, Taiwan, South Africa, Netherlands, Tanzania, United Kingdom, Pakistan, Australia, Ghana, Singapore, Nigeria, Turkey, Israel, Japan, Argentina, Egypt, India, Peru, South Africa, and Vietnam.

Regarding the level of evidence, more than half (51%) were classified as level VI, followed by IV (45%) and II (3%). Among the designs adopted, cross-sectional studies (51%) predominated, and, to a lesser extent, cohorts (25%), control cases (19%) and only one clinical trial (3%) were identified.

It was observed that in Brazil the amount of research on the theme is limited (three studies), of which two were developed based on cross-sectional design and a cohort. There was a lack of publications linked to nursing journals.

In response to the questioning of the present review, the results obtained were that the perinatal outcomes with the highest incidence in the duration of HSP were perinatal mortality (A1-2, 4, 6, 8-9, 12-15, 17, 20, 22-30), prematurity (A4, 6, 8-10, 12-15, 18, 22-25, 27-31), intrauterine fetal death (IUFD) (A17) and low APGAR in the 1st and 5th minute of life (A2, 4, 6, 8-10, 12, 16-17, 20-22, 27, 29-31). Likewise, outcomes such as NB Small for Gestational Age (SGA) (A1, 4, 10, 13-23, 25-31) were verified, with higher occurrence of admission to the Neonatal Intensive Care Unit (NICU) (A2, 4, 8-9, 15, 18-20, 22, 27), Intrauterine Growth Restriction (IUGR) (A3, 9, 16-17, 20, 24, 26) and cesarean delivery (A4, 14, 16-18, 27, 29, 31).

Following the aforementioned outcomes, results were also identified, such as neonatal...
sepsis (A10, 12, 26), Transient Tachypnea of NB (TTNB) (A19, 26), intraventricular hemorrhage (articles 10, 19), Meconium Aspiration Syndrome (MAS) (A3, 10, 21) and Respiratory Distress Syndrome (RDS) (A10, 21). The less frequently identified perinatal results were: pulmonary hemorrhage (A21), neutrophilia (A7), elevated thiobarbituric acid rate (TBARS) (A5), neonatal hypotension (A11), pneumonia (A26), icterus (A18), ischemic encephalopathy (A21), hypoglycemia (A19), and Necrotizing Enterocolitis (NEC) (A19).

In the studies, perinatal results in pregnant women diagnosed with PES were mentioned in 25 studies (80.6%), while in three, the identification of such outcomes was scored in cases that evolved with severity. In the other articles, perinatal results were identified in pregnant women with HP (12), HAC (11), Eclampsia (08), HELLP Syndrome (04) and CHOPE (01). It is noteworthy that in some studies, the same work investigated, simultaneously, the perinatal consequences in groups of pregnant women with different subtypes of HSP.

Table 1: Characterization of the articles regarding the identification, title and perinatal outcomes identified in the studies. Natal, Rio Grande do Norte, Brazil. 2017.
| A13 | Tan KH, Kwek K, Yeo GS. Epidemiology of pre-eclampsia and eclampsia at the KK Women’s and Children’s Hospital, Singapore. Singapore Med J. 2006;47(1):48-53. | Prematurity; Perinatal mortality; SGA / Low birth weight |
| A16 | Grisaru-Granovsky S, Halevy T, Eidelman A, Elstein D, IUGR; Caesarean; Low APGAR; Prematurity; SGA; Low birth weight | |


Acid rate
| A19 | Barton JR, Barton LA, Istwan NB, Desch CN, Rhea DJ, Stanziano GJ et al. Elective delivery at 34/0 to 36/6 weeks' gestation and its impact on neonatal outcomes in women with stable mild gestational hypertension. *Am J Obstet Gynecol.* 2011;204:44.e1-5. DOI: https://doi.org/10.1016/j.ajog.2010.08.030 | Prematurity; SGA / Low birth weight; NICU admission; Icterus |
## Discussion

Although the publication of research on the topic has been continuous over the past 15 years and in different countries, knowledge about perinatal outcomes in the presence of HSP, especially in the Brazilian context, remains an area that is still scientifically little explored, including nursing. Therefore, there is a need to encourage the development of studies that
address this issue, given the significant incidence of hypertension in pregnant women and the severity of it for the mother and the fetus/neonate.\textsuperscript{10}

In this review, perinatal mortality was identified as the most common negative result in women diagnosed with some type of hypertensive syndrome, which can be seen in studies A1-2, 4, 6, 8-9, 12-15, 17, 20 and 22-30. In Brazil, conditions originating in the perinatal period, including those resulting from maternal hypertensive disorders, stand out as the main cause of mortality during the period,\textsuperscript{11} although, these are considered conditions that can be reduced through adequate care for women during pregnancy, childbirth and the newborn.\textsuperscript{12}

Taking into account the ideas previously presented, conditions that originate in the perinatal period include respiratory and cardiovascular disorders; neonatal sepsis; disorders related to the duration of pregnancy and fetal growth, such as low birth weight and prematurity; as well as maternal complications that interfere with the usual evolution of pregnancy, labor, and delivery.\textsuperscript{11,13} These are recurring outcomes of the evolution of pregnancy in women with hypertension.

In the context of the Brazilian Unified Health System (in Portuguese, SUS), preventable causes of perinatal death are estimated to be those that would be preventable by the access and guarantee of a qualified assistance service during the pregnancy-puerperal cycle.\textsuperscript{12} Therefore, the synthesis of the studies shows that perinatal mortality presents itself as a persistent result in reality, even in the face of advances in care technologies and public policies for women’s health care.

Regarding specifically the occurrence of IUFD, a case-control study carried out in the city of Cuiabá, Mato Grosso do Sul (MG), Brazil, from 2006 to 2010, concluded that hypertensive maternal disorders were the second main cause responsible for fetal mortality, preceded only by unspecified causes.\textsuperscript{14}

Followed by perinatal mortality, prematurity (A 4, 6, 8-10, 12-15, 18, 22-25, 27-31) is the second most recurrent consequence in hypertensive pregnant women, agreeing with findings of
other studies, in which preterm birth was significantly associated with elevated blood pressure levels and, more often, with pre-eclampsia.\textsuperscript{7,15-16}

The conditions at birth, represented by the APGAR Index, appear to be worse depending on the type of HSP as verified in articles A2, 4, 6, 8-10, 12, 16-17, 20-22, 27 and 29-31. Thus, neonates of mothers with eclampsia have low APGAR scores up to the 5th minute,\textsuperscript{17} whereas those born to pregnant women with HP and PES were also born hypoxic, but less frequently.\textsuperscript{15,18} Despite the evidence found, a study did not identify a difference in APGAR between groups of NBs of hypertensive and normotensive mothers, and, based on this result, sought to emphasize that the index is affected by prematurity and congenital anomalies.\textsuperscript{6}

In the present study, 43.7\% of studies reported in their results an association between elevated maternal blood pressure levels and the presence of PES with low birth weight and SGA size (A 1, 4, 10, 13-23, 25-31).\textsuperscript{2,18} As a result of such adverse outcomes, admission to the NICU (A2, 4, 8-9, 15, 18-20, 22, 27) for special care, mainly due to asphyxia and prematurity, is seen with a considerable incidence in cases of hypertensive pregnant women.\textsuperscript{17-18}

Notably, the assistive technology of intensive care units has reduced mortality by allowing the recovery of debilitated newborns. However, manipulation by professionals and submission to interventions end up exposing the newborn to adverse events and risks that are harmful to their health, especially when hospitalization periods are prolonged.\textsuperscript{19}

Although IUGR is presented as the 6th most cited outcome in the research, as in papers A3, 9, 16-17, 20, 24 and 26, there is a consensus in the literature that its pathophysiology is closely related to maternal hypertensive disorders. PES, for example, promotes severe placental insufficiency, subjecting the fetus to hypoxia.\textsuperscript{12} In cases of CHOPE, growth restriction is also a common finding.\textsuperscript{20}

Nevertheless, elective termination of pregnancy in hypertensive pregnant women employing a cesarean section (A4, 14, 16-18, 27, 29, 31) remains a controversial subject in the
literature, although its occurrence is significant in cases that evolve with severity, as the PES.\textsuperscript{6,15}

According to conduct filed by the Ministry of Health (MS), the resolution of pregnancy is recommended only in situations where maternal and / or fetal conditions worsen, where conservative and / or expectant behaviors should preferably be adopted until the 34th week of pregnancy.\textsuperscript{21} When considering the available evidence to support the indication of cesarean sections in hypertensive pregnant women, a systematic review pointed out the respective criteria: “Fetal Heart Rate (FHR) not reassuring”, “oligohydramnios” and “Fetal centralization”, which are also indicated by the ministerial guidelines, and have a B of recommendation degree.\textsuperscript{22}

Neonatal sepsis also corresponded to a finding associated with neonates of mothers with HP,\textsuperscript{2} identified in articles A10, 12 and 26. There is a consensus in the literature that the etiology of infection during this period is multifactorial, covering factors related to maternal and neonatal conditions, such as premature labor, rupture of membranes over 18 hours, maternal infection, low birth weight, prematurity, mechanical ventilation (MV) with Orotracheal Tube (OTT), central or umbilical catheter and parenteral nutrition.\textsuperscript{23}

Studies have identified that the maternal duration of HP and CAH increases the risk for the occurrence of respiratory disorders such as TTNB (A19, 26), MAS (A3, 10, 21), RDS (A10, 21), in addition to hemorrhage and lung injury (A21) in preterm and low birth weight infants.\textsuperscript{2,12} It is observed that the complications mentioned above are closely related to the condition of prematurity since complications of this nature are secondary to preterm birth, which constitutes one of the main complications of HSP.

Neurological findings in premature newborns of hypertensive mothers are controversial and uncommon in research, the most frequent of which are intraventricular hemorrhage (A21), ischemic encephalopathy and periventricular leukomalacia.\textsuperscript{6} The frequency of complications such as NEC (A19), neutrophilia (A7), increased TBARS (A5), neonatal hypotension (A11),
pneumonia (A21), icterus (A18) and hypoglycemia (A19) were lower, but the consequences of these for neonatal health are of significant impact.

That said, NEC affects especially low birth weight preterms, constituting the most common clinical/surgical emergency and the biggest cause of NB morbidity and mortality in NICUs in the world.\textsuperscript{24} Its etiology is unknown, but it has associated factors such as prematurity, birth weight, asphyxia, sepsis, shock, mechanical ventilation, in addition to evidence that suggests its association with HP.\textsuperscript{25}

Biochemical changes such as neutrophilia elevated TBARS and hypoglycemia are noteworthy. A control case performed with infants of mothers with PE and normotensive revealed the activation of neutrophils in proportion to the severity of the hypertensive disease;\textsuperscript{26} whereas, concerning the increase of thiobarbituric acid, the detection of it in the urine of NBs of mothers with HG is constituted as a biomarker that assesses fetus exposure to chronic intrauterine hypoxia.\textsuperscript{27}

Hypoglycemia is commonly seen in macrosomal newborns and children of diabetic mothers, despite this, a study identified a significant incidence of hypoglycemia in neonates of mothers with HP.\textsuperscript{28} As for neonatal hypotension, this is a common problem in NICUs, especially in premature newborns, and, more recently, maternal PE has been associated with its occurrence.\textsuperscript{29} Finally, premature newborns of hypertensive mothers are associated with the neonatal diagnosis of icterus,\textsuperscript{30} since, among the risk factors for neonatal hyperbilirubinemia, prematurity is one of the outcomes considered recurrent in HSP.

Thus, the repercussions of HSP for perinatal outcomes are of significant impact, whether direct, as in the case of perinatal mortality, cesarean delivery, and prematurity; or indirect, such as the secondary outcomes to prematurity as low birth weight, admission to the NICU, sepsis, and others mentioned.
Conclusions

The most frequent perinatal outcomes during Hypertensive Syndromes in Pregnancy were: perinatal mortality, prematurity, low APGAR in the 1st and 5th minute of life, NBSGA, higher occurrence of admission to the NICU, IUGR and cesarean delivery.

Among the investigated hypertensive syndromes, the number of studies with pregnant women diagnosed with PE stood out, however, there was a smaller number of studies aimed at analyzing the perinatal outcomes in pregnant women with PES and CHOPE. Therefore, conducting investigations that analyze the exposure of the fetus/neonate to the maternal condition of both syndromes, constitutes a knowledge gap in the literature. Other types of HSP were researched such as HP, CAH, Eclampsia, and HELLP.

Taking into account the small number of studies carried out in Brazil, it is recommended that research could be carried out applying designs with a higher level of evidence, which aims to investigate the repercussions of HSP in the national context. This is because the socioeconomic profile of Brazilian women is consistent with elements considered to be risk factors for HSP, such as primiparity in women under 20 years of age, black, low educational level and poverty.

The review has as limitations the number of databases searched, the non-availability of non-free articles and the non-use of instruments to evaluate scientific articles.

References


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