

Review Article

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Anatomopathological Alterations of the Placenta with Preeclampsia: A Systematic Review

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ABSTRACT

The objective of this study was to carry out a systematic review that the amount of anatomopathological alterations in placentas from women who would develop PE would be higher compared to placentas from pregnant women without preeclampsia. In methods, for this systematic review, the keywords ("preeclampsia" and "placenta") were used, four databases were searched: SciELO, Lilacs, Google Scholar and Elsevier. In the results obtained, it is observed that, of the 86 registries identified, 6 were eligible. Other findings that, due to their frequency and maternal and fetal adverse outcomes, are very important: microscopic and macroscopic alterations, firstly, excess fibrin, secondly, abundant syncytial knots. Thirdly, infarctions. Within the macroscopic alterations of the placenta, we found low-weight placentas, and, finally, the evaluation of the methodological certainty of the six articles that entered the SR; they reached a score of >70%, classifying them as "sufficiently reported" articles. In conclusion, we say that the anatomopathological alterations that occur in the placenta lead to a dysfunctional, hypoxic, and ischemic placenta, causing PE and maternal, fetal and neonatal complication.

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Introduction

Every 3 minutes a woman dies in the world due to preeclampsia (PE), becoming a public health problem as it is one of the leading causes of maternal and neonatal death [1-3]. The incidence of preeclampsia worldwide is between 2 and 8% of all pregnancies [4]. In developing countries, the incidence is 2.4% and in developed countries 0.4% according to the WHO [5].

The Federation of Gynecology and Obstetrics (FIGO), defines preeclampsia in a woman with ≥ 20 weeks of pregnancy, systolic blood pressure ≥ 140 mm.Hg and diastolic blood pressure ≥ 90 mm.Hg in two measurements and with a interval of ≥ 4 hours, accompanied by proteinuria ≥ 300 mg in 24 hours, or protein/creatinine ratio > 30 mg/mmol, or 1 + dipstick protein, in a normotensive woman and completely resolved by 6 weeks postpartum [6,7].

In normal placentation, hemodynamic physiologic changes lead to adequate blood flow through the uterine arterioles. Fetal-derived cytotrophoblasts migrate through the decidua and myometrium to invade the endothelium and tunica media of the maternal spiral arteries, terminal branches of the uterine artery, which have become large, high-capacity, low-resistance vessels that supply blood to the fetus and mother. The placenta, connect the uterus with the intervillous space, giving rise to low resistance circulation, increased compliance and low vasomotor reactivity, facilitating free circulation [8,9].

Poor fetal vascular perfusion may be associated with umbilical cord obstruction such as hyper coiling. On histological examination, stenosis, dilation of the blood vessels, mural fibrin deposition in large fetoplacental veins, and low circulation in the most distal portions of the villous tree can be observed. Corangiosis is another vascular disorder that is produced by hyper capillarization of terminal villi. Hemorrhage and edema is characterized by loss of vascular integrity, which can affect large vessels and smaller vessels in the distal villi, the latter of which can present as intervillous thrombi [10].

The objective was to do a systematic review of the anatomopathological alterations of placentas with preeclampsia.

Methods

Search Strategy

The search strategy followed the recommendations of Berstock et al. we first selected keywords from selected articles, then used the Medical Subject Headings (MeSH) to find more related keywords with similar meanings: (preeclampsia" [MeSH Terms) and placenta (MeSH Term) and we used these keywords in all the searched databases and in the period from 2002 to 2022 [11]. Detailing in PUBMED/MEDLINE, the keywords were used with the following filters: full text, free, clinical trials, observational studies, human, female, languages English, Spanish and Portuguese. In the ScIELO, Lilacs, Google Scholar and ELSEVIER databases, the filters used were the same as in PUBMED. In the Pubmed database with the cited keywords, 214 articles were found and of these, after reading the title and abstract, 212 were excluded because they were review articles, 2 did not correspond to the theme/subject. None of the articles in the Pubmed database were selected to

participate in the study of this thesis.

In the SciELO database with the cited keywords, 58 articles were found, of which 7 were duplicates; 41 articles do not correspond to the topic, 9 articles are review; 1 article corresponds to the topic of study subject. In the Google Scholar database with these keywords, 784 articles that according to the article by (Muka 2019): 200 articles were taken for the review: 175 articles do not correspond to the topic; 24 were review articles; 1 article was a systematic review, none of these articles entered this study.

In the Lilacs database with these keywords, 127 articles were located: 29 were duplicates; 65 articles do not correspond to the topic; 27 articles were review articles; 1 systematic review and 5 articles entered this systematic review. In the Elsevier database with these keywords, 177 articles were found; They do not correspond to the topic 159; 15 articles were systematic reviews and 3 were review articles.

After reviewing all the databases, 6 articles were included in this systematic review.

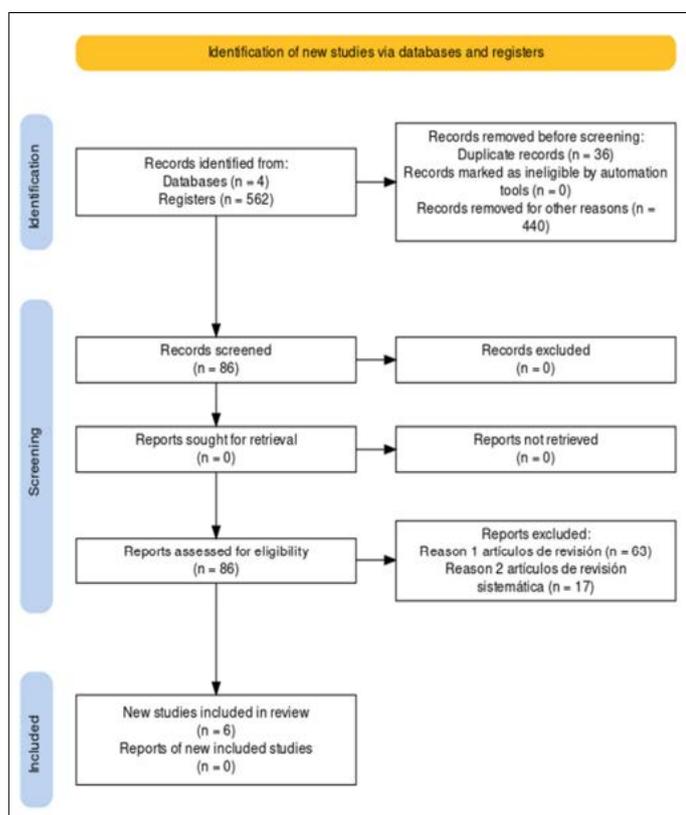


Figure 1: PRISMA 2020 Flow Diagram for New Systematic Reviews which included Searches of Databases and Registers only.

Inclusion Criteria

Pregnant women with preeclampsia and with pathological abnormalities of the placenta; Articles between the years 2002 to 2022; Articles with the languages English, Spanish and Portuguese; Free items; Articles that are type clinical trials; Observational articles in female humans.

Exclusion Criteria

Articles that, after reading the title and abstract, do not correspond to the theme/subject; Articles that are review; Type of articles that are systematic review; Duplicate articles in different databases. Prisma recommendation.

According to PAGE et al. in its guide article on writing a systematic review, it is described in the concept of P.I.C.O. in this thesis the description of PICO with a point is

P: of patients, corresponds to pregnant women with preeclampsia,
I: of intervention concerns women with preeclampsia,
C: of comparison between women; Pregnant women with preeclampsia and pregnant normotensive women,
O: means in English outcome,
which in Spanish indicates results of the thesis, whose topic is the anatomopathological alterations of the placenta with preeclampsia" [12].

Results

In five databases, with the keywords described in materials and methods, just reading the titles, 562 articles were found, of which 36 were eliminated for being duplicates and 440 for not being related to the research topic; after reading the titles and abstracts, 86 articles were excluded for other reasons; 69 articles are reviews, 17 are systematic reviews, in the end 6 articles were included in the study Figure 1.

In this investigation the authors decided to compare between pregnant women with hypertension and proteinuria; and normotensive pregnant women: It was observed that the group of patients with hypertension and proteinuria presented a mean maternal age (27 ± 7 vs. 29 ± 5) with no statistical difference, a greater number of nulliparous women (20 vs. 6), a lower number of multiparous women (14 versus 20) and higher.

Number of non-white women (27 vs. 11). Mean diastolic blood pressure was 106 mm. Hg for hypertensive pregnant women, compared to 80 mm. Hg for normotensive women. Among the patients with hypertension, the mean level of proteinuria was 1.6 ± 1.5 g at 24 hours. Hypertensive women gave birth at 32 weeks and normotensive women at 38 weeks with live newborns, appropriate for gestational age, whose mean weight was 1755 (± 831) in hypertensive women and 3155 (± 432) in normotensive women. children were born small for gestational age, statistically significantly higher in the hypertensive group (16 infants) than in the normotensive group (no infants).

When relating the density of micro vessels of the spiral arteries in the decidual and myometrial segments of the placental bed, between pregnant women with hypertension and proteinuria and normal pregnant women: It was observed that the placentas of women with hypertension and proteinuria had less micro vessel density Compared with placentas from normotensive women, both in the decidual zone (36.5 vs. 48.6) and in the myometrial segment (25.4 vs. 38.7), this difference was statistically significant. In addition, when comparing the density of the micro vessels of the spiral arteries in the decidual and myometrial segments of the placental bed, among hypertensive pregnant women according to diastolic blood pressure levels. It is considered that the density of the micro vessels of the spiral arteries was lower in hypertensive pregnancies (48.1 ± 13.0 versus 38.1 ± 11.9) (41.3 ± 14.8 versus 27.2 ± 14.3). (33.0 ± 6.8 vs. 25.4 ± 8.3) (27.8 ± 4.9 vs. 21.2 ± 5.3) with increased diastolic blood pressures (80-90mmHg) (90-100mmHg); (100-110mmHg) (110mmHg or more) micro vessel densities gradually decreased in both the decidua and myometrium with statistically significant difference.

Discussion

In our study, the main results of the articles that were included in this systematic review were microscopic alterations in the placentas of women with preeclampsia. Firstly, they had abundant

fibrin thrombi, fibrinoid material and fibrin. The second important result of the articles included in this thesis were syncytial knots. Finally, the third significant finding was a higher incidence of infarctions.

In this recent study De La Torre, et al, of a cross-sectional design, frequent microscopic alterations such as abundant syncytial nodules and infarcts were observed, coinciding with the articles that entered the systematic review, with the difference that this study was carried out at 3,600 m Tall. [13].

In the article by Abdelghany et al, in this new investigation, the observed microscopic lesions are similar to previous studies that are included in the systematic review, placentas with preeclampsia show numerous syncytial knots, other alterations differ from previous articles such as presence of thick-walled blood vessels, edematous spaces, fibrotic areas, and fibrinoid degeneration [14]. The microscopic examination of the placenta showed a decrease in the vessels in the terminal villi, an increase in syncytial knots and an increase in the perivillous fibrin deposit in the preeclampsia group in relation to the control group; the massive fibrin deposit is related to high perinatal morbidity and mortality and the formation of abundant syncytial knots is an advance for the pathophysiology of preeclampsia, information similar to that described in the articles that entered the systematic review.

In a study by Atigan et al, we observed massive presence of abundant perivillous fibrin, syncytial knots, significantly smaller blood vessels, hypo vascularization of the villi, cytotrophoblast proliferation, thickening of the trophoblastic membrane, increased size of the endothelial cells in the fetal capillaries, unlike what was observed in previous investigations [15].

In this current investigation, Pietro et al, found greater placental alterations in early preeclampsia than in late preeclampsia, predominantly the increase in syncytial ganglia, the deposit of perivillous fibrin, similar to previous studies, it was also observed that as the amount of fibrin deposits increased the frequency of PE in the groups, unlike in this study villous clumps, villous hypoplasia and decidual arteriopathy were observed with adverse maternal and neonatal outcomes than in preeclampsia [16].

Strengths

In this systematic review, the strengths of the study were the results found by the 6 studies included in the review, in which the most important results are the microscopic changes in pregnant women with preeclampsia and among these changes are the excess of fibrin in the placenta, which increases placental vasoconstriction and also produces necrosis of placental blood vessels. Another compelling result of the work was the increase in infarctions in the placenta of pregnant women with preeclampsia; it is known that infarction causes necrosis and death of placental tissue. In pregnant women with preeclampsia, syncytial knots increase, and this is harmful because it causes hypoxia, necrosis and reduction of both the placenta and blood vessels.

Limitations

The first limitation is the absence of a meta-analysis because there were no possible comparisons between the included studies. Another limitation is that the study did not present data collection and therefore does not have its own results and uses already published results and the third important limitation is related to the lack of studies related to the research topic.

Table 1: Qualitative Synthesis of the Results of the Studies included in this Systematic Review

Author	Year	Study design	Country	Sample size	Clinics and sociodemographic results	Microscopic results	Macroscopic results
Artico et al,	2009	cross	Brazil	76		Placental infarctions and hematomas were significantly frequent. Atherosclerosis with its changes histological was significant. Tenney Parker’s changes were moderate in placentas. hypertensive in relation to normotensive placentas	Average weight and volume of the placentas was low. The average number of clots and percentage of placental infarctions increased significantly
Cobo et al,	2021	Cases and control	México	52	The mean maternal age was higher in the cases compared to the controls. Caesarean section was common in the case group. The indications for cesarean section were preeclampsia with signs of gravity. The days of hospitalization were 144 days in the case group, due to prematurity.	Placental infarcts were frequent and similar in the four groups of PE, PE with IUGR, IUGR and normotensives. Accelerated villus maturation and syncytial knots were very common in preeclampsia with IUGR. Villous hypoplasia and syncytial knots were uncommon in IUGR. Fibrinoid was common in PE and in the PE with IUGR group	The weight of the placentas was significantly lower in the cases in relation to the group control, by far significant statistic. The weight of the newborn was statistically low

Coelho et al.	2006	cross	Brazil	60	Weeks of gestation It decreased with a statistical difference in hypertensive pregnant women with proteinuria in relation to normotensive women.	In hypertensive pregnant women with proteinuria, a significant decrease in the density of the micro vessels of the uterine spiral arteries is observed. When proteinuria is absent or decreased, micro vessel density. Increases.	The weight of the newborn decreased with a statistical difference in hypertensive pregnant women with proteinuria in relation to normotensive women.
Ekinci, et al.	2018	cross	Turkey	20	The number of live births was higher in normotensive women. In severe preeclamptic patients, they reveal that hemoglobin, as well as platelets, decreased and transaminases increased.	Cytotrophoblast cell degeneration is seen in severe PE. Increase in syncytial knots, fibrinoid necrosis. Endothelial cell degeneration, calcification, and hyaline hairy spots. In placentas with severe preeclampsia, Ki-67 expression was increased in decidual cells and inflammatory cells.	Macroscopic changes were not present in this study
Souza, et al.	2011	Cases and control	Brazil	28	The mean gestational age and Apgar score newborn was low in pregnant women with PE bought with pregnant women normotensive.	The area occupied by the fibrinoid increased 1.8 times more in PE than in controls. The areas occupied by the nuclei and the cytoplasm increased in the normotensive group. A decrease in the area occupied by the villi was reported in the PE group.	Mean newborn weight was low in women with PE.
Zapata et al.,	2021	cross	Colombia	200	Delivery by cesarean section was common in women with preeclampsia. Married and single women were frequently diagnosed with preeclampsia.	Calcifications and fibrin thrombi were very common. Placental infarctions, hemorrhage intervellosa and areas of maturation were frequent. Fibrin deposits and necrosis. were less frequent. In placentas with preeclampsia in relation to normotensive placentas	The weight of the placentas was similar in the preeclampsia group with a slight increase in the normotensive group.

Conclusions

We conclude that pregnant women with preeclampsia have many damages, including macroscopic and microscopic changes in the placenta, with increased fibrinoid in the placentas and increased infarction, impairing the function of this organ, resulting in low birth weight, restriction of the intrauterine growth, prematurity and a more adverse outcome may occur, such as neonatal death and even maternal death.

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