HYPERTENSION IN PREGNANCY

Hypertension in Pregnancy

ISSN: (Print) (Online) Journal homepage: www.informahealthcare.com/journals/ihip20

Effects of hypertensive disorders of pregnancy on the complications in very low birth weight neonates

Baoquan Zhang, Xiujuan Chen, Changyi Yang, Huiying Shi & Wenlong Xiu

To cite this article: Baoquan Zhang, Xiujuan Chen, Changyi Yang, Huiying Shi & Wenlong Xiu (2024) Effects of hypertensive disorders of pregnancy on the complications in very low birth weight neonates, Hypertension in Pregnancy, 43:1, 2314576, DOI: 10.1080/10641955.2024.2314576

To link to this article: https://doi.org/10.1080/10641955.2024.2314576

Published online: 20 Feb 2024.

HYPERTENSION IN PREGNANCY
2024, VOL. 43, NO. 1, 2314576
https://doi.org/10.1080/10641955.2024.2314576

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Effects of hypertensive disorders of pregnancy on the complications in very low birth weight neonates

Baoquan Zhang, Xiujuan Chen, Changyi Yang, Huiying Shi, and Wenlong Xiu

Neonatology Department, Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fuzhou, China

ABSTRACT

Objective: This study was designed to investigate the effects of hypertensive disorders of pregnancy (HDP) on the complications in very low birth weight (VLBW) neonates.

Methods: We retrospectively included VLBW neonates (<37 weeks) who were delivered by HDP pregnant women with a body weight of < 1,500 g (HDP group) hospitalized in our hospital between January 2016 and July 2021. Gestational age matched VLBW neonates delivered by pregnant women with a normal blood pressure, with a proportion of 1:1 to the HDP group in number, served as normal control.

Results: Then we compared the peripartum data and major complications between HDP group and control. The body weight, prelabor rupture of membrane (PROM), maternal age, cesarean section rate, fetal distress, small for gestational age (SGA), mechanical ventilation, RDS, necrotizing enterocolitis (NEC) (≥2 stage), Apgar score at 1 min, and mortality in HDP group showed statistical differences compared with those of the control (all $p < 0.05$). To compare the major complications among HDP subgroups, we classified the VLBW neonates of the HDP group into three subgroups including gestational hypertension group ($n = 72$), pre-eclampsia (PE) group ($n = 222$), and eclampsia group ($n = 14$), which showed significant differences in the fetal distress, Apgar score at 1 min, SGA, ventilation, RDS and NEC (≥2 stage) among these subgroups (all $p < 0.05$). Multivariate regression analysis showed that eclampsia and PE were the independent risk factors for SGA and NEC, respectively.

Conclusion: HDP was associated with increased incidence of neonatal asphyxia, fatal distress, SGA, mechanical ventilation, RDS, NEC and mortality. Besides, eclampsia and PE were independent risk factors for SGA and NEC.

ARTICLE HISTORY
Received 20 July 2023
Accepted 29 January 2024

KEYWORDS
Hypertensive disorders of pregnancy; hypertension; pre-eclampsia; eclampsia; very low birth weight neonate

Introduction

Hypertensive disorders of pregnancy (HDP), consisting of gestational hypertension, preeclampsia (PE) and eclampsia, and chronic hypertension with superimposed PE, are the most significant and intriguing problems in obstetrics (1), with a prevalence of 3%-5% among pregnant women worldwide. In developing countries, its prevalence is up to 15%, causing a mortality of 5 ~ 15% (2,3). Besides, HDPs are the leading risk factors for preterm birth (4). Therefore, it is a challenge for the health conditions of pregnant women and neonates.

Nowadays, the major maternal morbidities associated with HDP, in particular PE, include retinal detachment, cerebrovascular events, organ injury or even organ failure, as well as eclamptic seizures (5). Additionally, pregnancies complicated by HDP are associated with increased risk of stillbirth, low birth weight, fetal growth restriction, early neonatal death, placental abruption, neonatal asphyxia (6–8), as well as neonatal complications such as neonatal necrotizing enterocolitis (NEC) (9,10).

Very low birth weight (VLBW) serves as an important factor for child survival and long-term consequences such as non-communicable diseases. It has been accepted that addressing the factors associated with VLBW may reduce the mortality or morbidity. This leads us to investigate the potential relationship between HDP and the VLBW. This study was designed to understand the causes of the maternal and neonatal complications in VLBW neonates in HDP and normotensive pregnancies, with an aim to inform the future management strategies.

CONTACT Changyi Yang neo595@163.com Neonatology Department, Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, No. 18 Daoshan Road, Fuzhou 350001, China

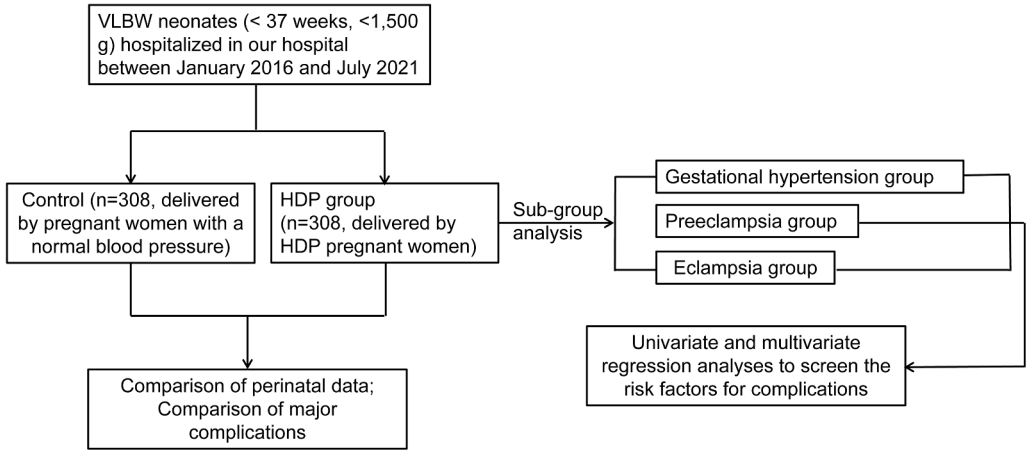

Figure 1. Study flowchart.

Table 1. Diagnostic criteria for pregnancy-associated hypertension.

Condition	Criteria Required
Gestational hypertension	BP > 140/90 mmHg after 20 weeks in previously normotensive women
Preeclampsia-	• ≥ 300 mg/24 h, or
Hypertension and:	• Protein: Cr ratio ≥ 0.3 or
Proteinuria	• Dipstick 1+ persistent[a]
Thrombocytopenia	or
Renal insufficiency	• Platelets < 100,000/μL
Liver involvement	• Creatinine >1.1 mg/dL or doubling of baseline[b]
Cerebral symptoms	• Serum transaminase levels[c] twice normal
Pulmonary edema	• Headache, visual disturbances, convulsions-
Eclampsia	• In a woman with preeclampsia, a convulsion that cannot be attributed to another cause. The seizures are generalized and may appear before, during, or after labor.

[a]Recommended only if sole available test; [b] No prior renal disease; [c]AST (aspartate aminotransferase) or ALT (alanine aminotransferase).

Materials and methods

Subjects

VLBW neonates (age <37 weeks; less than 1,500 g) who were delivered by HDP mothers (designated as HDP group) hospitalized in our hospital from January 2016 to July 2021 were included in this retrospective analysis (Figure 1). The diagnostic criteria for gestational hypertension, preeclampsia (PE) and eclampsia were given in Table 1 based on the Williams Obstetrics (24th Edition) (11). We excluded neonates with chromosomal abnormalities, severe congenital malformations and/or genetic metabolic diseases. Gestational age matched VLBW neonates delivered by pregnant women with a normal blood pressure, with a ratio of 1:1 in number to the HDP group, served as control group. Written informed consent was obtained from the parents or guardians. The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration. The study protocols were approved by the Ethical Committee of Fujian Maternal and Child Health Hospital (No.: 2017–502).

Data collection

The following data were collected from HDP group and control group: (i) maternal information: parity, number of fetus, blood pressure, utilization of antihypertensive drugs, premature rupture of fetal membrane (PROM), pregnancy complications, prenatal dexamethasone usage, delivery mode, as well as postpartum complications; (ii) neonatal information: gestational age, sex, birth weight, Apgar score at 1 min, small for gestational age (SGA), birth asphyxia, mechanical ventilation, neonatal respiratory distress syndrome (RDS), NEC, neonatal bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), and intraventricular hemorrhage (12); and (iii) neonatal death: death due to poor or even no responses to treatment, or critical illness. The Apgar score at 1 min was utilized to evaluate the effects of HDP on the neonatal conditions as previously described (12,13).

Univariate and multivariate regression analysis

To investigate the potential relationship between maternal HDP and neonatal complications, the VLBW neonates were classified into three subgroups according to the maternal HDP status, including gestational hypertension, PE, and eclampsia subgroups. Then we analyzed the variables in the three subgroups in the univariate regression analysis, and variables with a p value of less than 0.05 were subject to multivariate regression analysis to identify the independent risk factors for the VLBW.

Statistical analysis

Measurement data that were normally distributed were expressed as mean ± standard deviation. Inter-group differences were compared by two independent samples t-test or one-way analysis of variance (ANOVA). Enumeration data were described by frequency and percentage, and the differences between groups were compared by Chi square test. Multivariate logistic regression following univariate regression analysis was utilized to analyze the independent risk factors of major complications in HDP subgroups. SPSS 20.0 software was used for data analysis. A p value of less than 0.05 was statistically significant.

Results

Comparison of general information between HDP group and control group

There were statistical differences in the body weight, the prevalence of PROM, maternal age, birth weight, and cesarean section rate between HDP group and control group (all $p < 0.01$). No differences were noticed between the two groups in the male infant percentage, gestational age, in vitro fertilization-embryo transfer, primiparity, singleton pregnancy, prenatal dexamethasone, gestational diabetes mellitus (GDM), placental abruption and previa (all $p > 0.05$, Table 2).

Comparison of major complications between HDP group and control group

The incidence of fetal distress, SGA, mechanical ventilation, RDS, NEC (≥2 stage), Apgar score at 1 min, and mortality in HDP group showed statistical differences compared with those of the control (all $p < 0.01$, Table 3). There were no statistical differences in the BPD, ROP, intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), persistent pulmonary hypertension of the newborn (PPHN), cholestasis and sepsis between the two groups (all $p > 0.05$).

Comparison of major complications among the HDP subgroups

In this section, we classified the VLBW neonates of the HDP group into three subgroups including gestational hypertension group ($n = 72$), PE group ($n = 222$), and eclampsia group ($n = 14$). There were significant differences in the fetal distress, Apgar score at 1 min, SGA, mechanical ventilation, RDS and NEC (≥2 stage) among these three subgroups (all $p < 0.05$). No statistical difference was seen in the mortality among these subgroups ($p > 0.05$, Table 4).

Multivariate regression analysis on the preterm infant major complications

Multivariate regression analysis was performed after adjusting the gestational age, birth weight, sex,

Table 2. Comparison of general information between HDP group and control group.

Variables	HDP group ($n = 308$)	Control ($n = 308$)	t/χ^2	P value
Male neonates	148 (48%)	151 (49%)	0.058	0.809
Gestational age, weeks	30.8 ± 2.2	30.7 ± 2.1	0.781	0.435
Birth weight, g	1185.5 ± 217.2	1286.7 ± 177.2	6.331	$p < 0.001$
Maternal age, yrs	31.5 ± 5.8	29.7 ± 4.6	4.389	$p < 0.001$
In vitro fertilization-embryo transfer	41 (13.3%)	50 (16.2%)	1.044	0.307
Primiparity	99 (32.1%)	105 (34.1%)	0.264	0.607
Prenatal dexamethasone	279 (90.6%)	283 (91.9%)	0.325	0.569
Neonates delivered by GDM mother	79 (25.6%)	72 (23.4%)	0.430	0.512
PROM	43 (14.0%)	128 (41.6%)	58.487	$p < 0.001$
Caesarean section	241 (78.2%)	161 (52.3%)	45.827	$p < 0.001$
Placental abruption	44 (14.3%)	53 (17.2%)	0.991	0.319
Placenta previa	8 (2.6%)	14 (4.5%)	1.697	0.193

HDP, hypertensive disorders of pregnancy; GDM, gestational diabetes mellitus; PROM, premature rupture of fetal membrane. HDP group: VLBW neonates (age <37 weeks; birth weight < 1,500 g) delivered by HDP pregnant women. Control group: VLBW neonates delivered by pregnant women showing a normal blood pressure with matched gestational age.

Table 3. Comparison of major complications in HDP group and control.

Condition	HDP group ($n = 308$)	Control ($n = 308$)	t/χ^2	P value
Fetal distress	127 (41.2%)	74 (24%)	20.744	<0.001
Apgar score at 1 min	8.3 ± 2.2	8.9 ± 1.8	-3.212	0.001
SGA	152 (49.4%)	81 (26.3%)	28.161	<0.001
Mechanical ventilation	73 (23.7%)	51 (16.6%)	4.887	0.027
RDS	97 (31.5%)	68 (22.1%)	6.962	0.008
Sepsis	66 (21.4%)	49 (15.9%)	3.090	0.079
BPD	31 (10.1%)	32 (10.4%)	0.894	1.000
ROP	38 (12.4%)	26 (8.4%)	2.511	0.113
NEC, ≥2 stage	24 (7.8%)	11 (3.6%)	5.119	0.024
IVH	78 (25.3%)	86 (27.9%)	1.536	0.215
PVH	4 (1.3%)	3 (0.97%)	0.000	1.000
PPHN	0 (0%)	1 (0.3%)	/	1.000
Cholestasis	17 (5.5%)	11 (3.6%)	1.347	0.246
Death or predicted death	47 (15.3%)	28 (9.1%)	5.481	0.019

SGA, small for gestational age; RDS, respiratory distress syndrome; BPD, bronchopulmonary dysplasia; ROP, retinopathy of prematurity; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia; PPHN, Persistent pulmonary hypertension in the newborn. HDP group: VLBW neonates (age <37 weeks; birth weight < 1,500 g) delivered by HDP pregnant women. Control group: VLBW neonates delivered by pregnant women showing a normal blood pressure with matched gestational age.

Table 4. Comparison of major complications among the gestational hypertension group, PE group and eclampsia group.

Condition	Gestational hypertension ($n = 72$)	Pre-eclampsia ($n = 222$)	Eclampsia ($n = 14$)	F/χ^2	P value
Fetal distress	11 (15.3%)	109 (49.1%)	7 (50%)	26.130	<0.001
Apgar score at 1 min	8.4 ± 2.0	8.4 ± 2.1	6.4 ± 3.1	5.694	0.004
SGA	16 (22.2%)	128 (57.7%)	8 (57.1%)	27.668	<0.001
Mechanical ventilation	20 (27.8%)	46 (20.7%)	7 (50%)	7.107	0.029
RDS	15 (20.8%)	74 (33.3%)	8 (57.1%)	8.410	0.015
NEC, ≥2 stage	2 (2.8%)	19 (8.6%)	3 (21.4%)	6.324	0.042
Death	10 (13.8%)	33 (14.8%)	4 (28.6%)	2.050	0.359

SGA, small for gestational age; RDS, respiratory distress syndrome; NEC, neonatal necrotizing enterocolitis; HDP, hypertensive disease of pregnancy.

Table 5. Multi-variate regression analysis of major complications between the HDP subgroups.

	Gestational hypertension group			PE group			Eclampsia group		
Variables	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Fetal distress	0.5	0.220–1.134	0.097	0.729	0.432–1.230	0.236	1.41	0.306–6.489	0.659
Prenatal asphyxia	1.581	0.809–3.089	0.181	0.863	0.492–1.516	0.609	2.192	0.655–7.340	0.203
SGA	0.797	0.432–1.471	0.468	4.123	2.783–6.109	0.000	3.804	1.239–11.681	0.02
Mechanical ventilation	1.214	0.602–2.449	0.588	0.89	0.487–1.626	0.704	1.472	0.426–5.093	0.541
RDS	0.49	0.240–0.099	0.055	1.454	0.879–2.406	0.145	2.578	0.769–8.468	0.125
NEC, ≥2 stage	0.72	0.156–3.318	0.673	2.493	1.161–5.351	0.019	7.264	1.771–29.797	0.006
Death or predicted death	0.902	0.384–2.122	0.814	1.17	0.580–2.360	0.661	1.497	0.370–6.063	0.572

SGA, small for gestational age; RDS, respiratory distress syndrome; NEC, neonatal necrotizing enterocolitis; PE, pre-eclampsia; OR, odds ratio.

delivery mode, placental abruption, placenta previa, prenatal dexamethasone, GDM, neonatal asphyxia and maternal age. Our data showed that PE was an independent risk factor for SGA (OR = 4.123, 95% CI: 2.783–6.109) and NEC (OR = 2.493, 95%CI: 1.161–5.351) in the VLBW neonates. Eclampsia was an independent risk factor for SGA (OR = 3.804, 95%CI: 1.239–11.681) and NEC (OR = 7.264, 95%CI: 1.771–29.797) among the VLBW neonates (Table 5).

Discussion

The prevalence of HDP associated complications shows gradual increase worldwide (2–4,14). To date, more attention has been paid to the prevention and management of HDP, as well as the short- and long-term complications of preterm neonates. In perinatal fields, the mortality and morbidity rates of preterm neonates weighing less than 1,500 g are still high, and the survival rate is still low. Treatment of VLBW neonates is very important, which is also a topic

area in the perinatal fields. On this basis, we investigated the effects of maternal gestational hypertension on the VLBW neonates. In this study, we investigated the effects of HDP on the complications in VLBW neonates. We found that the HDP was associated with increased incidence of fatal distress, neonatal asphyxia, SGA, mechanical ventilation, hyaline membrane disease, NEC and mortality. Besides, multivariate regression analysis on the HDP subgroups showed that eclampsia and PE were the independent risk factors for SGA and NEC in VLBW neonates, respectively.

According to the previous studies (6,15,16), HDP patients presented shallow trophoblast invasion of the uterine spiral artery and coexistence of decidua vessels and intravascular trophoblast. Additionally, there might be extensive changes in the uterine spiral arteries such as vascular endothelial injury, insufficient protoplasm in vessel wall, endometrial cell proliferation and lipid accumulation, which may finally cause atherosclerosis (17). Atherosclerosis may cause stenosis and atresia of uterine spiral artery, which may result in decreased perfusion of placenta blood flow and inadequate supply of fetal nutrition (18). Eventually, it may cause intrauterine growth retardation, fetal growth restriction and SGA. In our study, compared with the control group, the birth weight was lower in HDP group, while the incidence of SGA was higher in the HDP group. After adjusting gestational age and gender, multivariate regression analysis indicated that PE and eclampsia were independent risk factors for SGA. In addition, there was a positive correlation between severity of HDP and the incidence of SGA. The incidence of SGA in the PE subgroup and eclampsia subgroup was significantly higher than that of the gestational hypertension subgroup.

HDP was closely associated with the increased risk of neonatal NEC (10). Lee et al. demonstrated that HDPs can trigger insufficient placental blood supply that can lead to intrauterine hypoxia, which may result in redistribution of fetal blood flow to ensure the supply of important organs (9). Therefore, the blood supply to the fetal brain, liver and other vital organs was preferentially guaranteed (19), while the blood supply to the intestinal tract and other secondary organs was insufficient. This may affect intestinal development, especially the formation of intestinal immune barriers. Consequently, the neonates delivered by HDP pregnant women show a high incidence of NEC. In this study, after adjusting the gestational age and gender, multivariate regression analysis indicated that PE and eclampsia were the independent risk factors for NEC. The incidence of NEC was the highest in the eclampsia subgroup, followed by PE and gestational hypertension subgroups.

The incidence of neonatal asphyxia, mechanical ventilation, RDS, and mortality in the HDP group showed statistical differences compared with that of control group. However, after adjusting the gestational age, birth weight and maternal factors, multivariate regression analysis indicated that HDP showed no significant effects on these conditions. For the reasons, it may be associated with the fact that more attention has been paid to the HDP in clinical practice, especially the pregnant women with PE. Thus, pregnant/fetal monitoring and active interference were recommended to prevent the progression of PE (20,21). Our data indicated that the majority of cases (90%) received hormonal therapy to ensure the pulmonary development, which could reduce the possibility of RDS induced by preterm delivery. In addition, most HDP patients underwent cesarean section in the HDP group, which implied that effective monitoring and interferences were given to the HDP pregnant women. For those confirmed with HDP, termination of pregnancy was given immediately, with an aim to reduce the possibilities of risks after ongoing pregnancy.

There are some limitations in this study. First, this is a single-centered retrospective study. Second, we did not include the treatment data of the HDP group into analysis. Third, the neonatal prognosis may be affected by different treatment regimens, which is not considered in our analysis.

Conclusions

In summary, we investigated the effects of HDP on the complications in VLBW neonates. HDP was associated with increased incidence of neonatal asphyxia, fatal distress, SGA, mechanical ventilation, RDS, NEC and mortality. Besides, eclampsia and PE were independent risk factors for SGA and NEC.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This study was supported by the Young Talent Program of Fujian Health Bureau [No. 2019-1-16, granted to Baoquan Zhang], and Sailing Project of Fujian Medical University [No. 2020QH1194, granted to Baoquan Zhang], and the Social Developmental Induction Program of Fujian Province [No. 2019Y0058, granted to Changyi Yang].

Article Highlights

- Effects of HDP on VLBW neonates.
- Eclampsia was a risk factor for SGA and NEC.
- PE was a risk factor for SGA and NEC.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author contribution

ZBQ and YCY contributed to conception and design of the study. CXJ, SHY and XWL organized the database. ZBQ performed the statistical analysis. ZBQ and CXJ wrote the first draft of the manuscript. YCY, SHY and XWL wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

References

[1] Ghulmiyyah L, Sibai B. Maternal mortality from preeclampsia/eclampsia. Semin Perinatol. 2012 Feb;36 (1):56–9. doi: 10.1053/j.semperi.2011.09.011

[2] Souza JP, Gülmezoglu AM, Vogel J, et al. Moving beyond essential interventions for reduction of maternal mortality (the WHO multicountry survey on maternal and newborn health): a cross-sectional study. Lancet. 2013 May 18;381(9879):1747–55. doi: 10.1016/S0140-6736(13)60686-8

[3] Chappell LC, Brocklehurst P, Green ME, et al. Planned early delivery or expectant management for late preterm pre-eclampsia (PHOENIX): a randomised controlled trial. Lancet. 2019 Sep 28;394(10204):1181–1190. doi: 10.1016/S0140-6736(19)31963-4

[4] Tong J, Niu Y, Chen ZJ, et al. Comparison of the transcriptional profile in the decidua of early-onset and late-onset pre-eclampsia. J Obstet Gynaecol Res. 2020 Jul;46(7):1055–1066

[5] Barry MJ, Nicholson WK, Silverstein M, et al. Screening for hypertensive disorders of pregnancy: US preventive services task force final recommendation statement. JAMA. 2023 Sep 19;330(11):1074–1082. doi: 10.1001/jama.2023.16991

[6] Phipps E, Prasanna D, Brima W, et al. Preeclampsia: updates in pathogenesis, definitions, and guidelines. Clin J Am Soc Nephrol. 2016 Jun 6;11(6):1102–13. doi: 10.2215/CJN.12081115

[7] Wadhwani P, Saha PK, Kalra JK, et al. A study to compare maternal and perinatal outcome in early vs. late onset preeclampsia. Obstet Gynecol Sci. 2020 May;63 (3):270–277

[8] Basta M, Hanif K, Zafar S, et al. Impact of hypertensive disorders of pregnancy on stillbirth and other perinatal outcomes: a multi-center retrospective study. Cureus. 2022 Mar;14(3):e22788

[9] Lee JY, Park KH, Kim A, et al. Maternal and placental risk factors for developing necrotizing enterocolitis in very preterm infants. Pediatr Neonatol. 2017 Feb;58 (1):57–62

[10] Yang CC, Tang PL, Liu PY, et al. Maternal pregnancy-induced hypertension increases subsequent neonatal necrotizing enterocolitis risk: a nationwide population-based retrospective cohort study in Taiwan. Med (Baltimore). 2018 Aug;97(31): e11739

[11] Cunningham FG, Leveno KJ, Bloom SL, et al. Williams obstetricsVol. 7. NewYork: McGraw-Hill Medical; 2015.

[12] Cloherty JP, Eichenwald EC, Stark AR. Manual of neonatal care. Philadelphia: Lippincott Williams & Wilkins; 2008.

[13] Genzel-Boroviczény O, Hempelman J, Zoppelli L, et al. Predictive value of the 1-min apgar score for survival at 23–26 weeks gestational age. Acta Paediatrica. 2010 Dec;99(12):1790–1794

[14] Kahsay HB, Gashe FE, Ayele WM. Risk factors for hypertensive disorders of pregnancy among mothers in Tigray region, Ethiopia: matched case-control study. Bmc Pregnancy Childbirth. 2018 Dec 6;18 (1):482.

[15] Wang A, Holston AM, Yu KF, et al. Circulating anti-angiogenic factors during hypertensive pregnancy and increased risk of respiratory distress syndrome in preterm neonates. J Matern Fetal Neonatal Med. 2012 Aug;25(8):1447–52

[16] San Juan-Reyes S, Gómez-Oliván LM, Islas-Flores H, et al. Oxidative stress in pregnancy complicated by preeclampsia. Arch Biochem Biophys. 2020 Mar 15;681:108255.

[17] Wang J, Guan C, Sui J, et al. Association between polymorphisms rs2228001 and rs2228000 in XPC and genetic susceptibility to preeclampsia: a case control study. Bmc Pregnancy Childbirth. 2021 Nov 22;21 (1):787. doi: 10.1186/s12884-021-04242-1

[18] Kim JY, Kim YM. Acute atherosis of the uterine spiral arteries: clinicopathologic implications. J Pathol Transl Med. 2015 Nov;49(6):462–71. doi: 10.4132/jptm.2015.10.23

[19] Kilavuz O, Vetter K. Is the liver of the fetus the 4th preferential organ for arterial blood supply besides brain, heart, and adrenal glands? J Perinat Med. 1999;27(2):103–106. doi: 10.1515/JPM.1999.012

[20] Witcher PM, Chez BF, Baird SM. Multisystem effects of hypertensive disorders of pregnancy: a comprehensive review. J Perinat Neonatal Nurs. 2015 Jul;29(3):229–239. doi: 10.1097/JPN.0000000000000114

[21] Garovic VD, August P. Preeclampsia and the future risk of hypertension: the pregnant evidence. Curr Hypertens Rep. 2013 Apr;15(2):114–21. doi: 10.1007/s11906-013-0329-4