Maternal Characteristics of Very Low Birth Weight and Extremely Low Birth Weight Incidence

Badar Muhammad Pajajaran, Herman Sumawan, Raden Tina Dewi Judistiani, Budi Handono

Department of Obstetrics and Gynecology, Faculty of Medicine, Padjadjaran University
Dr. Hasan Sadikin General Hospital, Bandung, Indonesia
Prof. Dr. Margono Soekarjo General Hospital, Purwokerto, Indonesia
Corresponding: dr.Badar Muhammad Pajajaran, Email : badarmpajajaran@yahoo.com

Abstract

Introduction: Low birth weight (LBW) infants have the potential for cognitive deficits, motor delays, cerebral palsy, and other behavioral and psychological problems. Household expenses and health care system costs can be reduced by alleviating the burden of LBW. Currently, there are no available data on the maternal characteristics of very low birth weight (VLBW) and extremely low birth weight (ELBW) incidence in Indonesia.

Method: This was a retrospective analytical observational study with a cross-sectional design. The sample in this study included all infants born with a birth weight of <1500 grams at Margono Purwokerto Hospital during 2018-2022. Univariate and bivariate analyses were performed using a significance level of $p \leq 0.05$.

Results: A total of 65 patients in the ELBW group and 59 patients in the VLBW group were included in this study. Statistical test results showed no significant differences in the characteristics of age, parity, birth weight of the infant, criteria for hypertension during pregnancy, criteria for anemia, comorbidities, hospital treatment, postpartum care, and type of delivery. The variables that differed significantly were anemia (Hb VLBW vs Hb ELBW; 9.06 vs 8.21) and neonatal outcomes.

Conclusion: There was no difference between the maternal characteristics of the incidence of very low birth weight and extremely low birth weight, except for anemia. Checking hemoglobin levels in patients with ELBW is essential for providing appropriate treatment.

Key words: very low birth weight infant, extremely low birth weight infant

Karakteristik Ibu dengan Bayi Berat Badan Lahir Sangat Rendah dan Kejadian Berat Badan Lahir Sangat Rendah

Abstrak

Pendahuluan: Bayi dengan berat badan lahir rendah (BBLR) berpotensi mengalami defisit kognitif, keterlambatan motorik, Cerebral Palsy, serta permasalahan perilaku dan psikologis lainnya. Pengeluaran rumah tangga dan biaya sistem pelayanan kesehatan dapat dikurangi dengan meringankan beban BBLR. Saat ini belum tersedia data mengenai karakteristik ibu dengan kejadian berat badan lahir sangat rendah (BBLR) dan berat badan lahir sangat rendah (BBLSR) di Indonesia.

Metode: Penelitian ini merupakan penelitian observasional analitik retrospektif dengan desain cross-sectional. Sampel dalam penelitian ini meliputi seluruh bayi yang lahir dengan berat badan lahir <1500 gram di RS Margono Purwokerto selama tahun 2018-2022. Analisis univariat dan bivariat dilakukan dengan tingkat signifikansi $p \leq 0,05$.

Hasil: Sebanyak 65 pasien pada kelompok BBLR dan 59 pasien pada kelompok BBLSR dilibatkan dalam penelitian ini. Hasil uji statistik menunjukkan tidak terdapat perbedaan bermakna pada karakteristik umur, paritas, berat badan lahir bayi, kriteria hipertensi saat hamil, kriteria anemia, penyakit penyerta, perawatan di rumah sakit, perawatan nifas, dan jenis persalinan. Variabel yang berbeda secara signifikan adalah anemia (Hb BBLSR vs Hb BBLR; 9,06 vs 8,21) dan luaran neonatal.

Kesimpulan: Tidak terdapat perbedaan karakteristik ibu terhadap kejadian berat badan lahir sangat rendah dan berat badan lahir sangat rendah, kecuali anemia. Pemeriksaan kadar hemoglobin pada pasien BBLR sangat penting untuk memberikan pengobatan yang tepat.

Kata kunci: bayi berat lahir sangat rendah, BBLSR, bayi berat lahir sangat rendah, BBLR

Introduction

The World Health Organization (WHO) defines low birth weight (LBW) as a birth weight of 2500 g regardless of gestational age. LBW is an important public health indicator for maternal health, nutrition, health service delivery, and poverty because LBW babies have a higher risk of death and disease immediately after birth and non-communicable diseases throughout their life. The pathophysiology of low birth weight (LBW) remains unclear, although intrauterine growth retardation (IUGR) and premature birth are considered causes of LBW.[1,2]

The World Health Organization classifies LBW based on gestational age into preterm (born before 37 weeks of pregnancy) and term (born after 37 weeks and before 42 weeks of pregnancy). These categories can each be separated into two groups based on whether they are small for gestational age (SGA) or not. Babies with low birth weight can also be classified into very low birth weight (VLBW) if the birth weight is less than 1500 grams and extremely low birth weight (ELBW) if the birth weight is less than 1000 grams.[1,3] Fetal genetic anomalies have an incidence of 5%–20% in IUGR cases. Fetal infection accounts for 5%–10% of IUGR cases. The most common causes of IUGR are cytomegalovirus and toxoplasmosis. The other infectious agents are varicella-zoster virus, malaria, syphilis, and herpes simplex. Fetuses with nonchromosomal congenital anomalies or specific syndromes may also experience growth restriction.[2,3]

Maternal morbidity can disrupt uteroplacental– fetal blood flow and cause IUGR. These conditions include chronic hypertension, gestational or pregestational diabetes mellitus, systemic lupus erythematosus, antiphospholipid syndrome, severe cardiopulmonary or renal disease, severe anemia and malnutrition, substance abuse, anti-neoplastic drugs or radiation exposure, chronic antepartum hemorrhage, pre-low gestational age or poor gestational weight gain, extreme maternal age, short interpregnancy interval, high altitude residency, multiple pregnancies, uterine malformations, and assisted conception. Maternal morbidity affects fetal growth through its adverse effects on placental function. On the other hand, placental and umbilical cord anomalies can cause IUGR. Maternal nutritional status can play a role in approximately 10% of the variation in fetal weight. Mothers who experience growth restriction have twice the risk of giving birth to IUGR neonates.[2,3] The prevalence of SGA IUGR varies among different populations. Prevalence rates of SGA IUGR are higher in resource-poor countries with the highest burden in South Asia, where up to 34% of babies are born with SGA IUGR.[4] IUGR is found in approximately 3%–7% of pregnancies. Incidence varies according to the population studied, gestational age of the fetus, and whether or not SGA fetuses were included. It is reported to be 6 times higher in underdeveloped and developing countries than in developed countries. Approximately 40% of IUGR cases are idiopathic, with no identifiable cause. Among the remaining 60% of cases with an identifiable cause, 1/3 are due to genetic disorders and the rest are secondary to environmental factors.[3,4]

To date, there are no data regarding maternal characteristics of very low birth weight (VLBW) and extremely low birth weight (ELBW) incidence in Indonesia. Therefore, this research will compare maternal characteristics in terms of the incidence of very low birth weight and extremely low birth weight at Margono Purwokerto Hospital in 2018-2022.

Method

Cross-sectional study with data from medical records of patients with babies born

with a body weight of 1500 g at Margono Purwokerto Hospital from 2018 to 2022. The sample size was determined using the unpaired categorical analytical research sample size formula and purposive sampling. Samples will be divided into two groups, namely, <1000 grams and <1500 grams. The minimum sample size for the two groups is 60 samples. Data were excluded if the baby was born with a weight of more than 1500 g or the medical record data was incomplete. The variables used in this study were maternal age, birth order, fetal weight at birth, hypertension criteria, anemia criteria, comorbidities, hospital treatment, postpartum care, neonatal outcomes, pregnancy complications, very low birth weight, and extremely low birth weight.

The data obtained were subjected to univariate and bivariate analyses to determine the data's frequency, distribution, and center. Univariate analysis was carried out on each variable with the final results being frequency and mean ± standard deviation. Bivariate analysis in this study was performed to compare the incidence of very low birth weight and extremely low birth weight at Margono Purwokerto Hospital in 2018-2022 using the chi-square test if the chi-square requirements are met with the alternative Fisher's exact test for Table 2 2 and Kolmogorov –Smirnov test for tables other than 2 2. The chi-square requirement is that there is no expected value less than 5 in 20% of the table. For numerical data, the p value is tested using the unpaired t- test if the data are normally distributed, and the alternative Mann –Whitney test if the data are not normally distributed. Bivariate analysis is considered significant if p p<0.05. All data were processed using SPSS© version 24.

Results

The total samples used in this study were 124 samples of 65 babies weighing <1000 grams and 59 babies weighing <1500 grams. A general description of maternal characteristics is presented in Table 1. In the group of babies weighing <1000 grams for the age group <20 years the prevalence was 4 or 6.2%, 20-35 years was 42 or 64.6% and >35 years was 19 or 29.2 %.

Categorical data analysis in table 1 was tested using the Chi Square Test on the variables of parity, gestational age, and fetal weight at birth as well as the alternative Kolmogorov –Smirnov test on the age variable, criteria for hypertension in pregnancy, and anemia criteria. From the statistical test results in the research group above, information on the P value for the variables age, parity, fetal weight at birth, criteria for hypertension in pregnancy, and anemia criteria was greater than 0.05 (P value >0.05).

Next, a comparison of comorbidities was performed in the two groups shown in Table 2. In the <1000 group, mothers with comorbid anemia were 13 or 20.0%, urinary tract infections (UTI) were 18 or 27.7%, hypertension was 37 or 56.9%, bleeding 5 or 7.7%, premature rupture of membranes 13 or 20.0%, premature contractions 14 or 21.5%, tuberculosis (TB) 1 or 1.5%, hepatitis 2 or 3.1%, and Coronavirus Disease 2019 (Covid-19) as much as 1 or 1.5%.

In the <1500 group, mothers with comorbid anemia were 23 or 39.0%, UTIs were 19 or 32.2%, hypertension was 31 or 52.5%, bleeding was 5 or 8.5%, premature rupture of membranes was 7 or 11.9%, premature contractions were 22 or 37.3%, tuberculosis was 0 or 0.0%, hepatitis was 0 or 0.0%, and COVID-19 was 0 or 0.0%.

Categorical data analysis in table 2 was tested using the Chi Square statistical test, namely anemia, UTI, hypertension, premature rupture of membranes, and premature contractions, as well as alternative Fisher's exact tests, namely bleeding, tuberculosis, hepatitis, and COVID-19. From

Table 1 Comparison of Maternal Characteristics

Variable	Group		Total N=124	p-value
	<1000 N=65	<1500 N=59		
Age				1.000
<20 years	4(6.2%)	2(3.4%)	6(4.8%)	
20-35 year	42(64.6%)	43(72.9%)	85(68.5%)	
>35 year	19(29.2%)	14(23.7%)	33(26.6%)	
Parity				0.113
1	17(26.2%)	20(33.9%)	37(29.8%)	
2	26(40.0%)	13(22.0%)	39(31.5%)	
3	13(20.0%)	11(18.6%)	24(19.4%)	
>3	9(13.8%)	15(25.4%)	24(19.4%)	
Gestational age				0.0001**
23-27 weeks	39(60.0%)	13(22.0%)	52(41.9%)	
28-32 weeks	20(30.8%)	30(50.8%)	50(40.3%)	
33-36 weeks	6(9.2%)	16(27.1%)	22(17.7%)	
Fetal weight at birth				0.075
501–600 grams	13(20.0%)	4(6.8%)	17(13.7%)	
601–700 grams	10(15.4%)	20(33.9%)	30(24.2%)	
701–800 grams	13(20.0%)	11(18.6%)	24(19.4%)	
801–900 grams	14(21.5%)	11(18.6%)	25(20.2%)	
901–1000 grams	15(23.1%)	13(22.0%)	28(22.6%)	
Criteria for hypertension during pregnancy				0.871
Chronic hypertension	3(4.6%)	1(1.7%)	4(3.2%)	
Gstational hypertension	0(0.0%)	7(11.9%)	7(5.6%)	
Superimposed preeclampsia	9(13.8%)	4(6.8%)	13(10.5%)	
Preeclampsia	4(6.2%)	4(6.8%)	8(6.5%)	
Severe preeclampsia berat	9(13.8%)	13(22.0%)	22(17.7%)	
Eclampsia	6(9.2%)	2(3.4%)	8(6.5%)	
No hypertension	34(52.3%)	28(47.5%)	62(50.0%)	
Anemia criteria				0.314
Severe anemia	0(0.0%)	2(3.4%)	2(1.6%)	
Moderate anemia	0(0.0%)	1(1.7%)	1(0.8%)	
Mild anemia	13(20.0%)	19(32.2%)	32(25.8%)	
No anemia	52(80.0%)	37(62.7%)	89(71.8%)	

Note: For categorical data, the p-value is calculated based on the chi-square test with the alternative Kolmogorov –Smirnov and Fisher's exact tests if the chi-square requirements are not met. Mark
Significance based on p-value <0.05.

Tabel 2 Perbandingan Komorbid para Kedua Kelompok

Variable	Group		Total N=124	p-value
	<1000 N=65	<1500 N=59		
Anemia	13(20.0%)	23(39.0%)	36(29.0%)	0.020*
Urinary tract infection	18(27.7%)	19(32.2%)	37(29.8%)	0.583
Hipertention	37(56.9%)	31(52.5%)	68(54.8%)	0.624
Bleeding	5(7.7%)	5(8.5%)	10(8.1%)	1.000
Premature rupture of the membrane	13(20.0%)	7(11.9%)	20(16.1%)	0.219
Premature contraction	14(21.5%)	22(37.3%)	36(29.0%)	0.054
TBC	1(1.5%)	0(0.0%)	1(0.8%)	1.000
Hepatitis	2(3.1%)	0(0.0%)	2(1.6%)	0.497
COVID-19	1(1.5%)	0(0.0%)	1(0.8%)	1.000

Note: For categorical data, the p value is calculated based on the chi-square test with the alternative Kolmogorov –Smirnov and Fisher's exact tests if the chi-square requirements are not met. Mark
Significance based on p value <0.05

Table 3 Comparison of Hospital Treatment, Post-partum care, and Neonatal Outcomes between the Two Groups

Variable	Group		Total N=124	p-value
	<1000 N=65	<1500 N=59		
Hospital treatment				0.113
Termination	35(53.8%)	40(67.8%)	75(60.5%)	
Konservative	30(46.2%)	19(32.2%)	49(39.5%)	
Postpartum care				0.862
Postpartum	42(64.6%)	39(66.1%)	81(65.3%)	
Intensive	23(35.4%)	20(33.9%)	42(34.7%)	
Neonatal outcomes				0.0001**
Stillbirth	15(23.1%)	5(8.5%)	20(16.1%)	
End	23(35.4%)	7(11.9%)	30(24.2%)	
PND	27(41.5%)	1(1.7%)	28(22.6%)	
Outpatient	0(0.0%)	46(78.0%)	46(37.1%)	
The types of Childbirth				0.444
Vaginal	32(49.2%)	25(42.4%)	57(46.0%)	
Cesarean section	33(50.8%)	34(57.6%)	67(54.0%)	

Note: For categorical data, the p-value is calculated based on the chi-square test with the alternative Kolmogorov –Smirnov and Fisher's exact tests if the chi-square requirements are not met. Mark
Significance based on p-value <0.05.

the results of statistical tests in the research group above, information on the P value for the variables UTI, hypertension, bleeding, premature rupture of membranes, premature contractions, tuberculosis, hepatitis, and COVID-19 was greater than 0.05 (P value >0.05).

Table 3 compares hospital treatment, postpartum care, neonatal outcomes, and type of delivery in the two groups. In the <1000 group, for patients receiving hospital treatment, the termination category was 35 or 53.8% and conservative was 30 or 46.2%. For patients with postpartum care in the postpartum category, there were 42 or 64.6% and intensive care,there were 23 or 35.4%. For patients with neonatal outcomes in the still birth category, there were 15 or 23.1%, end of life was 23 or 35.4%, perinatal death (PND) was 27 or 41.5%, and outpatient care was 0 or 0.0%. For patients with vaginal delivery, there were 32 or 49.2% and those with cesarean sections were 33 or 50.8%.

In the <1500 group, for patients with hospital treatment in the termination category, there were 40 or 67.8%, and conservative treatment was 19 or 32.2%. For patients with postpartum care in the postpartum category, there were 39 (66.1%) and intensive, 20 (33.9%. For patients with neonatal outcomes in the stillbirth category, it was 5 or 8.5%, end was 7 or 11.9%, PND was 1 or 1.7%, and outpatient was 46 or 78.0%. For patients with vaginal delivery, there were 25 (42.4%) and cesarean sections were 34 (57.6%.

Categorical data analysis (Table 3) was tested using the Chi Square Test on the variables hospital treatment, postpartum care, neonatal outcomes, and type of delivery. The results of the statistical tests in the research group above showed that the P value for the variables hospital treatment, postpartum care, and type of delivery was greater than 0.05 (P value> 0.05), which means it is not significant or not statistically significant, while the P value for the outcome variable neonates is smaller than 0.05 (P value <0.05), which means it is significant or statistically significant.

Discussion

In this study, there were no statistically significant differences in proportions between the variables age, parity, fetal weight at birth, hypertension criteria in pregnancy, and anemia criteria in the <1000 and <1500 groups; therefore, it can be concluded that the two groups are the same or there are no differences in characteristics at the start of the examination. This shows that the two groups are the same or homogeneous; therefore, they are suitable for comparison and further hypothesis testing.

Comparison of maternal comorbidities in the two groups showed that there were no statistically significant differences in proportions between the variables UTI, hypertension, bleeding, premature rupture of membranes, premature contractions, tuberculosis, hepatitis, and COVID-19 in the <1000 and <1500 groups.

Comorbid hypertension has the highest frequency (54.8%). Hypertension with complications, such as eclampsia and hemolysis syndrome, elevated liver enzymes, and low platelets (HELLP), was found in patients when they visited the hospital. Hypertension was found to be a risk factor for VLBW and ELBW.[2,5] The results showed that there were no significant differences in the hypertensive variable. This is in contrast to other studies that showed a significantly higher risk for VLBW ($\chi 2 = 9.415$; $P = 0.002$) and ELBW ($\chi 2 = 4.588$; $P = 0.03$).[5]

Hypertension is a common medical complication of pregnancy and is characterized by widespread vascular reactivity that predisposes to acute or chronic uteroplacental insufficiency, potentially resulting in prenatal and intrapartum fetal disorders. This condition can lead to several

adverse outcomes, such as IUGR, premature birth with accompanying complications, fetal death or an increased risk of perinatal death, edema, disseminated intravascular coagulopathy, placental abruption, acute kidney injury, hemolysis, increased liver enzymes, and low platelet counts. low, up to heart failure.[5,7]

Globally, pregnancy hypertension is the main cause of maternal and perinatal morbidity and mortality and accounts for approximately 12% of maternal deaths worldwide. 5 Preeclampsia, a pregnancy disorder characterized by hypertension (≥140/90 mmHg) and proteinuria (≥300 mg in urine 24 hours), affects 3%–4% of all pregnancies worldwide. Management of hypertension in pregnant women is needed to reduce the incidence of VLBW and ELBW. Magnesium sulfate can be used to prevent and reduce eclampsia risk. In addition, low-dose aspirin reduced the risk of preeclampsia by 17%, the risk of fetal or neonatal death by 14%, and the relative risk of preterm birth by 8%. Calcium supplementation can also be administered to prevent hypertensive disorders.[6,7]

In cases of severe hypertension, it needs to be managed with various agents to lower blood pressure, such as hydralazine, calcium channel blockers, methyldopa, diazoxide, prostacyclin, ketanserin urapidil, prazosin, isosorbide, and magnesium sulfate.[6,7]

The P value for the anemia variable was smaller than 0.05 (P value <0.05), which means that there was a statistically significant difference in proportion between the anemia variable in the <1000 and <1500 groups. These results agree with research conducted by Rocha et al., who showed that of 106 ELBW samples, 34 (32%) had anemia.[8] Lower blood hemoglobin (Hb) levels can reduce oxygen-carrying capacity to tissues and result in higher levels of organ dysfunction, including heart failure and inflammatory diseases.[8,9] Kanya et al. stated that low birth weight, mechanical ventilation, and hypotensive shock predict mortality in ELBW neonates, whereas low birth weight, lack of antenatal steroids, birth asphyxia, ventilation, and duration of oxygen therapy are predictors of major morbidity.[9]

Based on the development of anemia of prematurity, various factors play a role. One of the main causes of anemia of prematurity, especially in babies with very low birth weight (LBW, <1500 g), is a decrease in blood volume in the first few weeks of life, which ranges from 8.2 to 36.7 ml/kg per week.[8,10] Approximately 40% of VLBW babies and 90% of ELBW babies require red blood transfusions during the postnatal hospitalization period. In addition, decreased iron stores and low erythropoietin (EPO) levels influence the severity of anemia in prematurity.[9,10]

A impact of anemia of prematurity is iron deficiency. Iron is present in three forms in the baby's body. Most is present in erythrocytes as Hb (~66%-80%), the remainder is stored as ferritin and hemosiderin in the liver and spleen (~15%), and ~10% as circulating nonheme-storage iron bound to transferrin.[11] Iron flux is regulated by hepcidin, a negative regulator of iron that acts by limiting intestinal absorption and increasing iron retention in reticuloendothelial cells, via ferroportin (Fpn) or a transmembrane protein present in enterocytes and macrophages. The release of free iron via Fpn is important for iron absorption, recycling, and overall iron alignment. Transcription of hepcidin mRNA in the liver is inhibited under anemia conditions, resulting in increased absorption of iron from the duodenum and release of iron from macrophages.[11,12]

Most intrauterine iron transfers (75%) occur in the third trimester. ELBW babies are born before the third trimester of pregnancy; therefore, they do not receive vertical transfer of maternal iron stores and most of the fetal erythropoiesis occurs in the

womb.[11] Other maternal conditions such as obesity, gestational diabetes, hypertension, and placental failure in IUGR also limit iron transfer to the fetus.[11,13] Nearly 17% of premature babies are iron deficient at birth. Hb levels increase consistently by 0.21 g/dL between 22 and 40 weeks of gestation in the uterus. Fetal iron accumulates at 1.6–2.0 mg/kg/day and at birth, the total body iron stores are around 75 mg/kg, with 80% of total body iron contained in red blood cells at birth.[13]

The lifespan of red blood cells (RBC) is shorter in premature babies (~70 days) compared to adult RBC (~120 days). The need for increased RBC mass and expansion of circulating blood volume is also very much needed by premature babies as much as almost 3.47 mg of elemental iron per gram of Hb synthesized.[11,14] Red blood cell transfusions help reduce iron losses and can provide 0.5–1 mg iron per mL transfusion.[12]

In this study, treatment with termination was mostly performed in both groups. One of the reasons for termination is comorbidities such as hypertension. Termination is the definitive treatment for cases of preeclampsia regardless of gestational age. Induction of labor is used to terminate pregnancy in hypertensive mothers.[7,15] A study showed that the incidence of ELBW and VLBW is related to the management of serious cases of preeclampsia and eclampsia requiring active action in the form of immediate termination of pregnancy regardless of gestational age and estimated fetal weight. This results in the birth of babies with low birth weight.[15]

There was no statistically significant difference in proportion between the variables of hospital treatment, post-partum care, and type of delivery in the <1000 and <1500 groups. In contrast to the outcomes of neonates, which showed significant differences in proportions. Most ELBW cases die during the perinatal period. Perinatal death is defined as fetal death after 28 weeks of pregnancy and before 7 days after delivery.[16] The high mortality rate indicates the fragility of the ELBW group. Respiratory distress syndrome (RDS), intraventricular hemorrhage, pulmonary hemorrhage, and sepsis are the main causes of death, whereas RDS, hyperbilirubinemia, and sepsis are the most common morbidities during the neonatal period.[16,17]

Conclusion

There was no difference between the maternal characteristics of the incidence of very low birth weight and extremely low birth weight, except for anemia. Checking hemoglobin levels in patients with ELBW is essential for providing appropriate treatment.

References

1. Cutland CL, Lackritz EM, Mallett-Moore T, Bardají A, Chandrasekaran R, Lahariya C, et al. Low birth weight: Case definition & guidelines for data collection, analysis, and presentation of maternal immunization safety data. Vaccine. 2017 Dec 4;35(48 Pt A):6492–500.
2. K. C. A, Basel PL, Singh S. Low birth weight and its associated risk factors: Health facility-based case-control study. Pradhan PMS, editor. PLoS ONE. 2020 Jun 22;15(6):e0234907.
3. Osuchukwu OO, Reed DJ. Small for Gestational Age. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2023 Feb 9].
4. Chew LC, Verma RP. Fetal Growth Restriction. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2023 Feb 9].
5. Idris H, Duum NN, Adamu U, Abdullateef R, Yabagi I. Hypertensive disorders in pregnancy: Pattern and obstetric outcome in Bida, Nigeria. Niger Med J. 2020;61(1):42.
6. Brown CM, Garovic VD. Drug Treatment

of Hypertension in Pregnancy. Drugs. 2014 Mar;74(3):283–96.
7. Braunthal S, Brateanu A. Hypertension in pregnancy: Pathophysiology and treatment. SAGE Open Medicine. 2019 Jan;7:205031211984370.
8. Rocha G, Pereira S, Antunes-Sarmento J, Flôr-de-Lima F, Soares H, Guimarães H. Early anemia and neonatal morbidity in extremely low birth-weight preterm infants. The Journal of Maternal-Fetal & Neonatal Medicine. 2021 Nov 17;34(22):3697–703.
9. Mukhopadhyay K, Louis D, Mahajan G, Mahajan R. Longitudinal growth and post-discharge mortality and morbidity among extremely low birth weight neonates. Indian Pediatr. 2014 Sep;51(9):723–6.
10. Ohlsson A, Aher SM. Early erythropoiesis-stimulating agents in preterm or low birth weight infants. Cochrane Neonatal Group, editor. Cochrane Database of Systematic Reviews [Internet]. 2020 Feb 11 [cited 2023 May 19];
11. Raffaeli G, Manzoni F, Cortesi V, Cavallaro G, Mosca F, Ghirardello S. Iron Homeostasis Disruption and Oxidative Stress in Preterm Newborns. Nutrients. 2020 May 27;12(6):1554.
12. Bowen JR, Patterson JA, Roberts CL, Isbister JP, Irving DO, Ford JB. Red cell and platelet transfusions in neonates: a population-based study. Arch Dis Child Fetal Neonatal Ed. 2015 Sep;100(5):F411–5.
13. Kling PJ. Iron Nutrition, Erythrocytes, and Erythropoietin in the NICU: Erythropoietic and Neuroprotective Effects. NeoReviews. 2020 Feb 1;21(2):e80–8.
14. Fisher AL, Nemeth E. Iron homeostasis during pregnancy. The American Journal of Clinical Nutrition. 2017 Dec;106:1567S-1574S.
15. Khosravi S, Dabiran S, Lotfi M, Asnavandy M. Study of the Prevalence of Hypertension and Complications of Hypertensive Disorders in Pregnancy. OJPM. 2014;04(11):860–7.
16. Badran EF, Darwish RM, Khader Y, AlMasri R, Al Jaberi M, AlMasri M, et al. Adverse pregnancy outcomes during the COVID-19 lockdown. A descriptive study. BMC Pregnancy Childbirth. 2021 Dec;21(1):761.
17. Tagare A, Chaudhari S, Kadam S, Vaidya U, Pandit A, Sayyad MG. Mortality and Morbidity in Extremely Low Birth Weight (ELBW) Infants in a Neonatal Intensive Care Unit. Indian J Pediatr. 2013 Jan;80(1):16–20.