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Intrauterine Growth Restriction with and Without Pre-Eclampsia: Pregnancy Outcome and Placental Findings

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ABSTRACT

Background & Objective: Accordingly, this study aimed to assess pregnancy outcomes and pathological findings of the placenta caused by intrauterine growth restriction (IUGR) with or without pre-eclampsia (PE).

Materials & Methods: This cohort study was conducted on two groups: Group I was PE-induced IUGR (PE-IUGR), and group II was idiopathic IUGR (I-IUGR). Pregnancy and neonatal outcomes were evaluated in both groups. The placental assessment was also performed based on pathological findings. Data were compiled and analyzed by SPSS 21. An analytical study was conducted on the groups based on *t* (or non-parametric Mann-Whitney), chi-square, and Fisher's exact tests.

Results: The findings of this study showed that maternal age, body mass index (BMI), the incidence of preterm delivery, and low birth weight were higher in the PE-IUGR group (P<0.001 in all) than in the I-IUGR group, and the difference was statistically significant. Additionally, circulatory disorders and impaired anomalies were higher in the PE-IUGR group (P<0.001) than in the I-IUGR group.

Conclusion: Placental disorders and reduced blood flow to the fetus due to placental disorders might lead to low birth weight and preterm delivery.

Keywords: Intrauterine growth restriction, Placenta, Preeclampsia, Premature birth

Introduction

Intrauterine growth restriction (IUGR) is a condition in which a fetus fails to reach its normal growth potential **(1)**. IUGR is one of the most common pregnancy complications in developing countries, increasing neonatal morbidity and mortality **(2)**. Its prevalence is 7%-15% globally and 30% in developing countries (including Iran) **(3, 4)**. One of the most important causes of IUGR is early-onset pre-eclampsia (PE). Still, IUGR with normal blood pressure and without any obvious reason (i.e., idiopathic IUGR [I-IUGR]) is also common **(5)**. IUGR in PE is 3 to 4 times more than normal. Even in some studies, PE is considered as a factor for the occurrence of IUGR **(6)**.

PE is defined as blood pressure above 140/90 and the occurrence of proteinuria in the second half of pregnancy **(7, 8)**. In other words, PE is a syndrome characterized by the onset of hypertension and proteinuria; or hypertension and end-organ damage that happens with or without proteinuria after 20 weeks of gestation **(9)**. The pathophysiology of PE includes maternal, fetal, and placental factors. Placental dysfunction is generally considered to be one of the leading causes of severe cases of IUGR. PE is divided into two categories: early- and late-onset PEs. Late-onset PE is occurred at 34 weeks of gestation and is accompanied by normal fetal development. Early-onset PE occurs before the 34th week of gestation and is characterized by IUGR **(10)**.

The term PE/IUGR is associated with either normal or minimal pathological findings and described as maternal—and not placental—disease **(11)**. PE and

IUGR are the main reasons for perinatal mortality and morbidity **(11)**.

PE/IUGR leads to preterm delivery before 34 weeks of gestation. Placental pathology (such as thrombotic villous) is a common finding in early-onset PE/IUGR **(12)**.

Both early-onset IUGR and early-onset PE are indicators of placental pathology, which is associated with hypoxia and circulatory damage due to placental dysfunction and obstruction of spiral arteries. Some common injuries include infarction, inflammation, and lesions such as chronic ischemia. Maternal Hypertension can be associated with early-onset IUGR, which leads to abnormal Doppler **(8, 13, 14)**.

Maternal hypertension and/or abnormal placental Doppler can be associated with early-onset IUGR, which both are associated with poor perinatal outcomes **(15, 16)**.

Doppler studies have also illustrated that early-onset PE/IUGR is associated with an effect on the spiral arteries, as these arteries' defects can play a much lesser role near the term **(17)**. Motawea *et al.* found a compelling association between high levels of α_2-adrenergic receptors (α_2-ARs) and pregnancy-related pathologies of severe PE and IUGR. Besides, Motawea claimed that human placenta-expressed α_2-ARs might be implicated in the pathogenesis of PE and IUGR **(18)**. Hypoxia of the placenta in PE is a powerful stimulus for the vascular endothelial growth factor (VEGF).

It has been proved that the increased secretion of VEGF proteins affects hypoxia and atherosis of the placental **(19)**. PE-induced IUGR (PE-IUGR) and I-IUGR share common histological changes, suggesting similar pathogenesis. Maternal malperfusion lesions predominated in PE-IUGR with fetal vascular malperfusion were higher in I-IUGR than in PE-IUGR. Hofbauer cells (HBCs) increased in both PE-IUGR and I-IUGR **(20)**. Thus, it seems that PE-IUGR can be accompanied by a normal trophoblastic transformation in the first trimester and atherosclerotic changes in spiral arterioles later. Late changes lead to increased mass in placental, especially in diabetic and twin pregnancies; indeed, placental changes can be found in prolonged pregnancies, placental edema, and fetal hydrops necrosis **(21, 22)**. Awamleh *et al.* found placental microRNA (miRNA) as an effective potential factor on gene expression and pathophysiology of early-onset PE and IUGR **(23)**.

This study was designed to compare the pregnancy outcomes and placental pathological findings in IUGR of two groups with and without PE in patients referred to Alzahra Hospital in Rasht (Iran) between 2018 and 2019.

Materials and Methods

IUGR was examined in pregnant women referred to Alzahra Hospital in Rasht (Iran) in this cohort study. Based on Doppler sonography, which is defined as birth weight under 10% percentile of birthweight curves for gestational age, pregnant women with IUGR were divided into two groups of high blood pressure (PE-IUGR, exposed) and normal hypertension (I-IUGR, unexposed) during pregnancy. PE was defined based on the American College of Obstetricians and Gynecologists (ACOG).

This study was confirmed/approved by the Research Council/Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1397.453). Before being enrolled in the study, pregnant women and their husbands gave their informed consent. Patients with known structural or chromosomal anomalies or intrauterine infections were excluded from the study. Information such as maternal characteristics and neonatal outcomes were obtained from all patients through a questionnaire.

Maternal characteristics were age, gestational age, gravidity, parity, body mass index (BMI), number of cigarettes smoked per day, type of delivery, and known diseases (including diabetes, chronic hypertension, thrombophilia, seizure, and asthma).

Neonatal outcomes were Apgar scores of less than 7 in 5 min, hospitalization duration, and neonatal intensive care unit (NICU) hospitalization. Early neonatal complications are usually as follows: blood transfusion, sepsis, respiratory distress, mechanical ventilation, seizure, phototherapy, intraventricular hemorrhage, respiratory support, hypoxic-ischemic encephalopathy, or death.

In this study, all the pathological assessments of the placenta were performed in the laboratory of Alzahra Hospital by the same pathologist who was not aware of the outcomes of pregnancies and randomization. Sample groups were based on the standard protocol presented in previous studies **(24)**.

After removing membranes and the umbilical cord, the placenta was fixed in formalin and weighed. For each placenta, a minimum of eight tissue samples from areas with abnormal appearance were obtained, including one sample from the entrance of the umbilical cord, one from the middle of the placenta tissue with abnormal macroscopic appearance, two grossly abnormal samples from the center of the tissue, one sample from an abnormal placental margin, an extra-sample of membranes, and two samples from the umbilical cord. Paraffin block was prepared and evaluated microscopically. The fetoplacental weight ratio (neonatal birth weight to placental weight ratio) was also measured.

Maternal- or fetal-originated placental lesions were defined based on the Pediatric Pathology Society. Lesions were divided into three pathophysiological groups: lesions with abnormal maternal blood flow, lesions with abnormal fetal vascular support, and inflammatory lesions. Maternal circulatory lesions are divided into several categories; in the first category, the

continuity of maternal blood circulation is reduced by retro placental hemorrhage. The second category of vascular injuries is associated with insufficient maternal perfusion (acute atherosclerosis and mural hypertrophy). The third category of villi changes is associated with maternal under-perfusion (increased syncytial knots, agglutination of villi, increase in fibrin deposition of villi, and infarction of villi). Fetal vascular support lesions were thrombo-occlusive vascular lesions (including chorionic vascular thrombosis and primary villi vessels) and vascular lesions associated with vascular occlusive diseases (fibrotic, hypovascular, and avascular villi).

Placental findings, including chorioamnionitis, are defined as infiltration of neutrophil inflammatory cells at more than two spots on the chorionic surface and extracellular membrane. The maternal inflammatory response is divided into three stages: early and subacute chorioamnionitis (stage 1), acute chorioamnionitis (stage 2), and late and severe chorioamnionitis (stage 3). The fetal inflammatory response is also divided into three stages, including early (stage 1), moderate arthritis of the umbilical arteries (stage 2), and concentrated umbilical vacuities (necrotizing funisitis; stage 3). In addition, when the lymphocyte (inflammatory cells) are infiltrated in the stroma or terminal of the villi, inflammation of the villi with unknown cause or chronic villitis is generated, which usually spreads to small vessels.

The current study included placental features reported according to the latest pathology criteria in the cases mentioned above.

In order to compare pregnancy outcomes and placental findings in PE-IUGR and I-IUGR groups with 95% CI and 80% test power, the sample size was determined based on the study by Kovo *et al*. **(24)**. The mean placental weight in neonates born in the PE-IUGR and I-IUGR groups was 314±106 and 348±74, respectively, and, according to the sampling formula, at least 108 subjects in each group were evaluated.

In this study, data were collected, coded, and entered into SPSS 21 (SPSS Inc., Chicago, Ill., USA) Mean and SDs (95% CI) were used to describe quantitative variables with normal distribution, and interquartile ranges were used for quantitative variables with abnormally-distributed. Qualitative variables were also described based on number and percentage. Normal distributions of the study variables were measured using the Kolmogorov-Smirnov Test.

Analytical evaluation and comparison of pregnancy outcomes and placental findings in the PE-IUGR and I-IUGR groups were performed based on *t* (or Mann-Whitney non-parametric equivalent) and chi-square tests (when Fisher's exact test was not valid) in order to identify the effect of independent risk factors (maternal age, BMI, gestational age, birth weight, etc.). A logistic regression model was used for neonatal outcomes in the presence of one or more complications, such as blood transfusion, sepsis, respiratory distress, mechanical ventilation, seizure, phototherapy, intra-ventricular hemorrhage, respiratory support, hypoxic-ischemic encephalopathy, or death. The level of statistical significance of the tests was considered as a P-value<0.05.

Results

In the present study, 216 cases with IUGR were studied after being divided into 108 cases with PE (PE-IUGR) and 108 cases without PE (I-IUGR).

Maternal characteristics are presented in Table 1. As can be seen, the average age of the mothers was higher in the PE-IUGR group than in the I-IUGR group. However, this difference was not statistically significant (*P*=0.193). Gestational age based on the time of birth and ultrasound confirmation was significantly lower in the PE-IUGR group than in the I-IUGR group (*P*=0.001). BMI was higher in the PE-IUGR group than in the I-IUGR group. However, this difference was not statistically significant (*P*=0.491). There were no smokers in the current study.

Table 1. Maternal characteristics in two groups (with & without PE)

Variable	PE-IUGR (n=108) mean±SD median (min-max)	I-IUGR (n=108) mean±SD median (min-max)	P-value
Maternal age (year)	6.44±30.18 30.00 (45-17)	6.16±28.92 29.00 (45-16)	*0.193
Missing data (n)	2	2	
Gestational age at birth time (week)	3.25±31.92 33.00 (39-27)	5.16±32.92 34.00 (40-16)	*0.001
Missing data (n)	1	1	
Gestational age due ultrasonography(week)	2.57±35.16 36.00 (40-24)	4.38±35.59 36.00 (41-15)	*0.033
Missing data (n)	1	0	
BMI (Kg/m^2)	5.38±29.67 29.30 (40.06-16.33)	5.18±29.31 28.84 (40.12-19.53)	*0.491
Missing data (n)	2	6	

Variable	PE-IUGR (n=108) mean±SD median (min-max)	I-IUGR (n=108) mean±SD median (min-max)	P-value
Gravidity (n)	0.56±1.67 2.00 (3-1)	1.12±1.69 1.00 (6-1)	*0.068
parity	0.51±0.32 0 (2-0)	0.61±0.39 0 (2-0)	*0.613
Birth weight (gram)	584.33±1863.42 2020.0 (3570.0-500.0)	826.38±2376.46 2400.0 (3890.0-460.0)	**0.001>
Missing data (n)	1	9	

* Mann -Whitney Test
** Chi-square Test

There was no statistically significant difference between the groups in terms of gravidity (*P*=0.068) and parity (*P*=0.613). According to the results, the percentage of cesarean section was significantly higher in the PE-IUGR group (88%) than in the I-IUGR group (75.7%; *P*=0.020). There was no statistically significant difference between the two groups in terms of diabetes (*P*=0.353) and asthma (*P*=0.818). Chronic hypertension was significantly higher in the PE-IUGR group (95.4%) than in the I-IUGR group (4.6%; *P*<0.001). Seizures were also observed only in four cases in the PE-IUGR group. Thrombophilia was not observed in any cases. Birth weight was significantly lower in the PE-IUGR group than in the I-IUGR group (*P*<0.001).

According to the results, the presence of the opacity in thefetal surface of the placenta was more in the PE-IUGR group than in the I-IUGR group (24.8% vs. 15.2%). However, this difference was not statistically significant (*P*=0.053). There was no significant difference between the two groups regarding examining the fetal surface of membranes (*P*=0.234). In terms of the maternal surface of the placenta, the observed difference between the two groups was statistically significant (*P*=0.001; Table 2).

At birth, 8.4% of the PE-IUGR group had an Apgar score of less than seven, while in the I-IUGR group, it was 19.4%; this difference was statistically significant (see Table 3).

Using log-binomial regression analysis among maternal characteristics, gestational age (by modulating the effect of other identified variables) was directly related to early neonatal outcomes (…[Adjusted Rrlative Ratio]=0.899; 95% CI, 0.813-0.995; *P*=.039; Table 4).

Table 2. Placental characteristics (with & without PE)

Variable		PE-IUGR (n=108)	I-IUGR (n=108)	p value
Fetal surface of the placenta n (%)	**grist**	76 (75.2)	81 (81.8)	**0.053
	opaque	25 (24.8)	15 (15.2)	
	meconium	0	3 (3.0)	
Missing data (n)		7	9	
Fetal surface of the membrane n (%)	**complete**	75 (75.0)	66 (67.3)	*0.234
	in complete	25 (25.0)	32 (32.7)	
Missing data (n)		8	10	
Maternal surface n (%)	**Opaque**	36 (36.0)	50 (50.0)	**0.001
	Dark with calcification	10 (10.0)	13 (13.0)	
	Dark without calcification	26 (26.0)	17 (17.0)	
	Pale	8 (8.0)	12 (12.0)	
	Rigid	20 (20.0)	4 (4.0)	
	Bright red	0	3 (3.0)	
	Fibrin	0	1 (1.0)	
Missing data (n)		8	8	
Velamentous length n (%)	**40 cm>**	9 (8.3)	17 (17.2)	*0.055
	40-70 cm	99 (91.7)	82 (82.8)	
Missing data (n)		0	9	
Cord appearance n (%)	**True knot**	4 (4.7)	2 (2.3)	**0.446
	torsion	2 (2.4)	1 (1.2)	

Variable		PE-IUGR (n=108)	I-IUGR (n=108)	p value
	hemorrhage	1 (1.2)	0	
	gray	78 (91.8)	83 (96.5)	
Missing data (n)		23	22	
Membrane appearance n (%)	**complete**	7 (6.9)	21 (20.6)	**0.002
	incomplete	3 (3.0)	3 (2.9)	
	translucent	83 (82.2)	61 (59.8)	
	opaque	8 (7.9)	17 (16.7)	
Missing data (n)		7	6	
Cord vessels n (%)	**Normal**	104 (96.3)	98 (99.0)	**0.371
	Abnormal	4 (3.7)	1 (1.0)	
Missing data (n)		0	9	
Placental parenchyma n (%)	**Normal**	23 (21.3)	50 (49.0)	*0.001>
	Abnormal	85 (78.7)	52 (51.0)	
Missing data (n)				
Membranes parenchyma n (%)	**Normal**	107 (99.1)	86 (84.3)	*0.001>
	Abnormal	1 (0.9)	16 (15.7)	
Missing data (n)		0	6	
Cord parenchyma n (%)	**Normal**	101 (93.5)	90 (92.8)	*0.835
	Abnormal	7 (6.5)	7 (7.2)	
Missing data (n)		0	11	

* Chi-square Test
**Fisher's Exact Test

Table 3. Fetal characteristic in two groups (with & without PE)

Variable		PE-IUGR (n=108)	I-IUGR (n=108)	p value
Fetal weight mean±SD median(min-max)		606.73±1754.93 1800.0 (3250.0-339.0)	918.34±2139.65 2300.0 (3900.0-157.0)	**0.001
Missing data (%)		2	6	
Fetal gender n (%)	**Female**	**63 (58.3)**	60 (55.6)	*0.680
	Male	**45 (41.7)**	48 (44.4)	
Fetal number n (%)	**one**	**102 (94.4)**	93 (86.1)	*0.039
	two	**6 (5.6)**	15 (13.9)	
Apgar score ≤7 in 5 min n (%)	**Yes**	**9 (8.4)**	21 (19.4)	*0.020
	No	**98 (91.6)**	87 (80.6)	
Missing data		1	0	
NICU hospitalization n (%)	**Yes**	**73 (68.2)**	66 (61.1)	*0.275
	No	**34 (31.8)**	42 (38.9)	
Missing data		1	0	
NICU duration of hospitalization mean±SD median(min-max)		7.16±5.31 4.00 (30-0)	5.85±4.62 4.00 (24-0)	**0.431
Missing data		2	0	
Duration of hospitalization mean±SD median(min-max)		0.47±0.68 1.00 (1-0)	1.29±0.75 1.00 (13-0)	**0.601
Missing data		3	1	
Blood transfusion n (%)	**Yes**	**6 (5.6)**	1 (0.9)	***0.065
	No	**101 (94.4)**	107 (99.1)	
Missing data		1	0	

Variable		PE-IUGR (n=108)	I-IUGR (n=108)	p value
Phototherapy n (%)	**Yes**	**(9.3) 10**	(11.1) 12	*0.669
	No	**(90.7) 97**	(88.9) 96	
Missing data		1	0-	
Respiratory distress n (%)	**Yes**	**(33.6) 36**	(23.1) 25	*0.088
	No	**(66.4) 71**	(76.9) 83	
Missing data		1	0	
Death n (%)	**Yes**	**(3.7) 4**	(9.3) 10	*0.097
	No	**(96.3) 104**	(90.7) 98	
Early neonatal complications n (%)	**Yes**	**(40.7) 44**	(36.1) 39	*0.484
	No	**(59.3) 64**	(63.9) 69	
Missing data		1	0	

* Mann -Whitney Test
** Chi-square Test
*** Fisher's Exact Test

Table 4. Logistic-binomial regression analysis results of factors associated with neonatal outcomes

Variable	ARR[1]	Max SD[2]	P-value	95% Confidence interval	
				Lower	Upper
Maternal age (year)	1.003	0.0149	0.826	0.974	0.033
Birth age (week)	0.899	0.0514	0.390	0.813	0.995
BMI	0.990	0.0244	0.690	0.944	1.039
Gravidity	1.085	0.1785	0.648	0.765	1.539
C/S	1.428	0.3201	0.266	0.762	2.673
Pre-eclampsia	1.121	0.2641	0.664	0.668	1.882
Birth weight (gr)	1.000	0.0003	0.260	1.000	1.001

1-Adjusted Relative Ratio 2- Maximum Standard Deviation

Discussion

In this cohort study, pregnant women with IUGR were divided into two groups: one with normal blood pressure (I-IUGR) and the other with high blood pressure (PE-IUGR). This classification was made based on the findings of Doppler ultrasound. As mentioned before, they were examined for pregnancy outcomes and pathological findings of the placenta.

In the present study, the rates of placental parenchymal disorders and early neonatal complications were observed. The rates were significantly higher in the PE-IUGR group than in the I-IUGR group. Women with PE have a three- to four-fold increased risk of IUGR **(6)**. In some studies, PE has even been considered as a factor for the exacerbation or occurrence of IUGR **(9, 25, 26)**.

In the present study, the average age of mothers was higher in the PE-IUGR group than in the I-IUGR group, but it was not significant (*P*=0.193). Findings indicate that higher maternal age during pregnancy might increase the likelihood of maternal complications **(24)**. Gestational age was significantly lower in the PE-IUGR group than in the I-IUGR group (*P*=0.001). Low gestational age at birth can be the result of circulatory disorders and fetal hypoxia. Also, the BMI of mothers was higher in the PE-IUGR group than in the I-IUGR group (*P*=0.491). Besides, these results are consistent with the outcomes of a study by Kovo *et al.*, who found that mothers with higher BMI were more likely to have high blood pressure **(24)**.

There was no statistically significant difference between the two groups in terms of gravidity and parity. According to the results, the rate of cesarean section was significantly higher in the PE-IUGR group (88%) than in the I-IUGR group (75.7%). Higher cesarean section rates in the PE-IUGR group may indicate the possibility of fetal distress and the need for rapid termination of pregnancy. The cause is impaired blood and oxygen supply to the fetus **(2)**.

There was no statistically significant difference between the two groups in terms of diabetes, seizures, and asthma. This discrepancy will probably be seen in studies with larger sample sizes.

Birth weight was 1863.42±584.33 g in the PE-IUGR group and 2376.46±826.38 g in the I-IUGR group; it was significantly lower in the PE-IUGR group than in the I-IUGR group. Most studies have shown similar results **(24)**. The above-mentioned findings might indicate the

effect of the underlying disease on weight gain and fetal growth **(9)**. It also occurs earlier in patients with hypertension due to higher placental abnormalities **(25)**.

There was no statistically significant difference between the two groups in terms of gender. The above finding indicates that high blood pressure does not affect fetus gender. There was no significant difference between the two groups in terms of the fetus number. According to this result, the influence of blood pressure on the number of fetuses is insignificant.

The need for neonatal intensive care unit (NICU) hospitalization was higher in the PE-IUGR group (68.2%) than in the I-IUGR group (61.1%); however, this difference was not statistically significant.

There was no statistically significant difference between the two groups regarding NICU hospitalization and overall hospitalization duration.

The need for blood transfusion was seen in 5.6% and 0.9% of cases in the PE-IUGR and I-IUGR groups, respectively. As said before, there was a higher need for blood transfusion in the PE-IUGR group. These findings can indicate the effect of high blood pressure on neonatal complications.

Bernstein *et al*. conducted a study on a population of 19,759 neonates with very low birth weight and without major anomalies and showed that IUGR was strongly associated with neonatal death, necrotizing enterocolitis, and respiratory distress syndrome **(2)**.

In the PE-IUGR group, the placental surface was cloudy in 24.8% of cases, while in the I-IUGR group, this rate was 15.2%. According to the above findings, the possibility of IUGR might increase in placental disorders.

In a study by Gerretsen *et al*., similar results were obtained **(27)**. Normal umbilical cord length (40-70 cm) was seen in 91.7% of PE-IUGR and 82.8% of I-IUGR participants. This difference was not statistically significant. There is a possibility that this result may change if more comprehensive research is conducted. The study of the umbilical cord showed that the number of true, twisted, and bleeding nodes was more in the PE-IUGR group than in the I-IUGR group. According to these results, it can be concluded that impaired blood supply might lead to IUGR.

The results of a study conducted by Eger *et al*. confirmed the results of the present study. There was a statistically significant difference in the appearance of membranes in the two groups. The above finding might indicate the effect of placental abruption on IUGR and the effect of hypertension on the placenta **(16)**.

According to the placental parenchymal investigation results, 78.3% and 51% of cases were abnormal in the PE-IUGR and I-IUGR groups, respectively; this difference was statistically significant. In this finding, the effect of placental disorders on IUGR and the impact of blood pressure on the placenta can be seen **(9)**. The results of the membrane parenchyma examination showed that the parenchymal membrane was normal in 99.1% and 84.3% of cases in the PE-IUGR and I-IUGR groups, respectively; this difference was statistically significant. Similar results have been observed in a study conducted by Kovo *et al*. **(24)**. Normal parenchym of umbilicus was observed in 93.5% and 92.8% of cases in the PE-IUGR and N-FGR groups, respectively; this difference was not statistically significant.

Generally, among maternal characteristics, gestational age was directly related to preterm neonatal outcomes by modulating the effect of other identified variables. This finding is consistent with the results of other studies.

The results of this study were similar to the results of Benton et al.study regarding the effect of placental pathology on IUGR **(28)**. Kovo *et al*. showed pregnancy outcomes and placental findings in complicated pregnancies with IUGR and with or without PE. They also examined delivery results, fetal and neonatal outcomes, and pathological parameters of the placenta in under 10% percentile of birthweight-curve neonates and gestational age of 24-42 weeks. It was concluded that older women with hypertension had higher BMI compared to.normotensive younger women. Thus, the preterm birth rate (before 34 weeks) was higher in patients with normal blood pressure **(25)**; the present study showed similar results. Women with PE had more IUGR, poorer pregnancy outcomes, and worse vascular injuries of the maternal placenta compared with those without PE. Also, the results of circulatory disorders and placental parenchyma disorders were similar to the study conducted by Kovo *et al*. **(14)**.

Conclusion

The present study results demonstrated that mothers with IUGR and high blood pressure had higher rates of preterm delivery, lower birth weights, and premature neonatal complications than mothers with normal blood pressure. Also, in these patients, placental parenchymal damage was worse than mothers with normal blood pressure; this confirms the effect of blood pressure on placental function and consequently on fetal growth. According to the present study results, among maternal characteristics, gestational age is related to early neonatal outcomes independently. Also, the results of this study proved the importance of blood pressure control of pregnant women and the need for more care for mothers with high blood pressure and IUGR.

Limitations of our study were the small sample size and failure to assess the incidence of involved biochemical markers.

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Conflict of Interest

The authors report no conflicts of interest in this work.

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