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ORIGINAL ARTICLE

Comparison of Retinopathy of Prematurity Incidence in Preterm Infants of Mothers with Preeclampsia and Infants of Healthy Mothers

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Abstract

Introduction Preeclampsia is one of the four leading causes for pregnancy complications, maternal–fetal and neonatal mortality. This study was aimed at comparing the incidence of retinopathy of prematurity in neonates of mothers with preeclampsia and neonates of healthy mothers.

Methods This cross-sectional study was performed among 213 mothers, including 49 healthy mothers and 164 mothers with preeclampsia whose neonates were admitted to the neonatal intensive care unit of Ghaem Hospital, Mashhad, Iran, during 2016–2021. The participants were chosen using the convenience sampling method. The data collection tool was a researcher-made checklist including items on laboratory evaluation, maternal and neonatal characteristics, and eye examination. The data were analyzed using *t*-test and Chi-square.

Results In the two groups, gestational age ($P=0.112$), first-minute Apgar score ($P=0.209$), and fifth-minute Apgar score ($P=0.949$) were not significantly different. There was a significant difference between the two groups in terms of maternal age ($P=0.0001$), type of delivery ($P=0.0001$), premature rupture of membranes ($P=0.003$), and eye condition ($P=0.033$).

Conclusion The results of our study show that preeclampsia affects the prognosis of infants, and in neonates with preeclamptic mothers, the rate of premature rupture of the membranes, cesarean delivery, and retinopathy of prematurity were higher.

Keywords Preeclampsia · Neonatal · Retinopathy of prematurity · Premature rupture of membranes

Introduction

BP greater than 140/90 mmHg after 20 weeks of gestation plus proteinuria greater than or equal to 300 mg in 24 h or protein to creatinine ratio greater than or equal to 0.3 or a stable + 1 result in the urine dipstick test and hepatic involvement as an increase in serum transaminases is considered preeclampsia [1]. Preeclampsia is a complex disorder that affects about 5–8% of pregnant women after the 20th week of pregnancy [2]. The World Health Organization estimates that 7–8% of women aged 14 to 59 years in the East Mediterranean region suffer from preeclampsia [3].

In Iran, in recent years, the prevalence of preeclampsia has increased, while the prevalence of eclampsia has decreased. Thus, it seems that in future, preeclampsia and its complications will be considered as a serious public health concern [4]. In Zabol, the prevalence of preeclampsia was 6.5%. Serious maternal complications related to this condition include hepatic impairment (13.1%), renal impairment (3.1%), transfusion (4.6%), thrombocytopenia (2.3%), visual impairment (2.3%), and hemolysis, elevated liver enzymes, and low platelets syndrome (0.8%), while the neonatal complications include prematurity (29.2%), meconium amniotic fluid (12.3%), Apgar score of below 7 at birth (7.7%), and stillbirth (0.8%) [5]. Preeclampsia is also one of the four leading causes of perinatal death [6]. It is still one of the most significant unresolved issues in obstetrics leading to some pregnancy complications and maternal–fetal, and infant mortality [2].

Numerous studies have been performed concerning the prognosis of maternal preeclampsia. Some studies did not

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show any adverse harmful effects more common and also can be used effects on neonates of preeclamptic mothers [7]. However, most studies have reported several complications of these mothers' infants, including intrauterine weight loss, oligohydramnios, intrauterine death [8], neonatal thrombocytopenia, neutropenia, decreased number of T-regularity cells, increased natural cytotoxic killer cells, and hearing impairment [6, 9]. Few studies have been carried out on the subject of effects of preeclampsia on the incidence of premature rupture of membranes (PROM), birth status, and the incidence of Retinopathy of prematurity (ROP).

Retinopathy of prematurity (ROP) occurring in premature infants is mostly mild and moderate, and as the child grows, it gradually improves. Treatments such as laser or Avastin injection may hinder the possible complications. Severe ROP and retinal detachment have a poor prognosis and even surgery may not solve the problems. Retinopathy of prematurity is one of the major etiologies of blindness in childhood, which is significantly affected by oxygen. To reduce the ocular problems of premature infants, the risk factors for ROP need to be controlled. Meanwhile, the accurate and frequent control of premature infants and their follow-up tests lead to an early diagnosis and appropriate treatment and reduction of future problems in these children.

Treatment becomes more challenging, and the risk of complications grows with the increased severity of the disease. Proper treatment is required in cases of stage 3, 4, and plus ROP, as delayed treatment may cause ocular complications, such as blindness [10, 11].

Due to dissimilarity in the findings of previous studies on the role of preeclampsia in the prognosis of neonates, including the incidence of ROP. In this cross-sectional study, we decided to compare the long-term prognosis of rupture of membranes, type of delivery, first-minute Apgar score, fifth-minute Apgar score, and retinopathy of prematurity (ROP) in neonates of mothers with preeclampsia and neonates of healthy mothers.

Methods

This cross-sectional study was performed on 213 mothers including 49 (23%) healthy mothers without diabetes, chronic hypertension, epilepsy, hypothyroidism, thrombocytopenia, vascular collagen disease, infectious diseases, preeclampsia, or other known diseases during pregnancy and 164 (77%) mothers with preeclampsia whose neonates were admitted to the neonatal intensive care unit of Ghaem Hospital in Mashhad during 2016 to 2021. The participants were chosen using the convenience sampling method. Ghaem Hospital is a general referral hospital with a NICU [12 beds], a Level 2 care [25 beds], and a maternity ward (Level 1 care) with about 3,000 deliveries per year.

The checklist was completed based on complete maternal (i.e., maternal age, parity, gestational age, type of delivery, and premature rupture of membranes) and neonatal (i.e., first-minute Apgar score, fifth-minute Apgar score, and eye condition) history. In clinical medicine, the diagnostic criteria for preeclampsia are defined as following: BP greater than 140/90 mmHg after 20 weeks of gestation in women who previously had normal blood pressure, proteinuria greater than or equal to 300 mg in 24 h, protein to creatinine ratio of greater than or equal to 0.3, stable + 1 result in urine dipstick test, hepatic involvement as serum transaminases twice as normal or pulmonary edema [1]. Premature preterm rupture of the membranes (PPROM) and the loss of amniotic fluid is considered before the onset of labor pains in pregnancies under 37 weeks [12].

Newborns are screened for ROP at 32 weeks of gestation or four weeks after birth. The classification of ROP stages is based on the international classification. To explain the posterior and anterior extension, the eye is divided into three zones with Zone I being the most posterior and Zone III the most anterior.

Zone I: A circle whose center corresponds to the disk, and its radius is twice the distance from the disk to the macula.

Zone II: Starting at the end of Zone I and continuing to Ora serrata on the nasal side and approximately to the equator on the temporal side.

Zone III: The rest of the retina, which consists of the upper and lower temporal areas and is located in front of Zone II [13].

Type 1 threshold disease is described as stage 3 ROP in zone I or zone II for a minimum of five consecutive hours or eight non-consecutive hours in total, is described as plus disease. Plus disease, which is an indicator of the severity of the disease, is defined as dilatation and tortuosity of the posterior pole arteries of the eye.

First, using statistical tables, we described the results, and then using Chi-Square and *t*-test in SPSS version 20, we compared the two groups of neonates with preeclamptic mothers and neonates of healthy mothers. A *P*-value of less than 0.05 was considered significant.

Results

The present study was performed on 213 mothers including 49 (23%) healthy mothers and 164 (77%) mothers with preeclampsia. On eye examination, 69 (32.4%) neonates had normal examination, and 144 (67.6%) neonates had ROP. The mean gestational age in the neonatal group with preeclamptic mothers was 31.64 ± 1.97 weeks, and in neonatal group with healthy mothers, it was 32.40 ± 3.14 weeks. In the two groups, maternal age ($P = 0.0001$) was significantly different, but gestational

age ($P = 0.112$), first-minute Apgar score ($P = 0.209$), and fifth-minute Apgar score ($P = 0.949$) were not significantly different (Table 1).

Chi-square test showed a statistically significant relationship between preeclampsia and type of delivery ($P = 0.0001$), eye condition ($P = 0.033$), PROM ($P = 0.035$), and neonatal resuscitation ($P = 0.045$). This means that in infants with preeclamptic mothers, there were higher rates of cesarean delivery, PROM, need for neonatal resuscitation, and ROP (Table 2).

Discussion

In this study, despite the homogeneity of gestational age in the two groups, the incidence of ROP in neonates of preeclamptic mothers was 20% higher than in neonates of healthy mothers. Studies to determine the association of preeclampsia with ROP have reported conflicting results. Yu [14] and Seiberth's study [15] showed that preeclampsia is associated with a reduced risk of ROP in preterm infants, possibly due to the impact of oxidative stress on fetal growth [16]. In Shulman*'s* study, preeclampsia was associated with an increased risk of ROP [17]. In Shah's study, maternal preeclampsia was also a predictor of ROP in

Table 1 Comparison of the two groups of neonates with preeclamptic mothers and neonates of healthy mothers

Variable	Neonates of preeclamptic mothers 164 preeclamptic mothers (77%) Mean ± SD	Neonates of healthy mothers 49 healthy mothers (23%) Mean ± SD	*Significance level (*t*-test)
Maternal age (years)	31.19 ± 6.04	27.82 ± 6.47	0.0001
Parity	2.12 ± 1.34	2.10 ± 1.37	0.920
Gestational age (weeks)	31.64 ± 1.97	32.40 ± 3.14	0.112
First-minute Apgar score	6.62 ± 2.13	7.04 ± 1.69	0.209
Fifth-minute Apgar score	8.21 ± 1.61	8.23 ± 1.30	0.949

Table 2 Comparison of some maternal and neonatal variables in the two groups of neonates with preeclamptic mothers and neonates of healthy mothers

Groups variables	Neonates of preeclamptic mothers 164 preeclamptic mother (77%)	Neonates of healthy mothers 49 Healthy mothers (23%)	*Significance level (Chi-square test)
Premature rupture of membranes			
Yes	42 (25.6)	4 (9.18)	0.035
No	122 (74.4)	45 (90.82)	
Type of delivery			0.001
Normal delivery	23 (14.1)	24 (48.9)	
Cesarean section	141 (85.9)	25 (51.1)	
Neonatal resuscitation			0.045
Yes	44 (26.8)	6 (12.2)	
No	120 (73.2)	43 (87.8)	
Sex			0.395
Male	89 (54.3)	22 (44.9)	
Female	75 (45.7)	27 (55.1)	
Eye examination			0.032
Healthy	47 (28.7)	22 (44.9)	
ROP	117 (71.3)	27 (55.1)	
ROP			0.023
Normal	61 (37.2)	29 (59.3)	
ROP1	50 (30.5)	6 (12.1)	
ROP2	50 (30.5)	14 (28.6)	
ROP3	3 (1.8)	0 (0)	

*$P < 0.05$ was considered significant

very-low-birth-weight infants [18]. In Ozkan*'s* study, maternal preeclampsia was associated with an increased risk of ROP in preterm infants. Retinopathy of prematurity was also more severe in infants born to preeclamptic mothers [19], possibly due to the impact of ischemic and angiogenic stress on retinal vascularization [20]. The lack of regulation of Anti-angiogenic factors plays a critical role in the pathogenesis of preeclampsia and ROP [21]. According to a study, increased oxidative stress combined with elevated pro-inflammatory cytokine levels in infants born to preeclamptic mothers may interfere with the normal growth of retinal vessels in vulnerable retinas [22]. On the other hand, preeclampsia, if severe, can lead to significant prematurity of the baby, which in return, affects the outcomes of the infants' vision due to the severity of prematurity [14].

In this study, the rate of caesarean section in preeclamptic mothers was estimated about 35% higher than in healthy mothers. In Bursal Duramaz**'s** study, which compared the prognosis of 140 neonates of preeclamptic mothers with 144 neonates of healthy mothers, caesarean delivery was more frequent [23]. In Pacher**'s** study, the most common type of delivery for women with preeclampsia was elected caesarean section [24]. The results of Sukmawati's study indicated that, at present, cesarean delivery is highly prevalent in cases of preeclampsia, severe preeclampsia, and complicated preeclampsia [25]. In Xu's study, cesarean section rate in patients with severe preeclampsia was approximately 66%. Although the only treatment for preeclampsia is the termination of pregnancy, deciding on the type of delivery is not easy. Obstetricians and gynecologists are often concerned about the deteriorating clinical condition of the mother and fetus during vaginal delivery. Therefore, many patients and physicians choose caesarean delivery [26].

In the present study, PROM in preeclamptic mothers was more common than in healthy mothers. In several studies, gestational hypertension and preeclampsia have been associated with an increased risk of PROM [27, 28]. In the study of Boskabadi et al., between 3% and 9.5% of PROM cases had preeclampsia [29, 30]. It can be hypothesized that PROM, just like preeclampsia, is associated with an increased humoral immune response to the fetus, and therefore, there is a potential for impaired immune tolerance to fetal alloantigens [31].

The most important limitation of the study was the lack of long-term follow-up of ROP and the lack of management of preeclampsia.

Conclusion

Our findings reveal that preeclampsia affects the prognosis of infants, such as that in infants with preeclamptic mothers, the rates of cesarean delivery, ROP, and PROM were higher. Therefore, timely diagnosis and appropriate treatment of pregnant women with a diagnosis of preeclampsia are essential to prevent the occurrence of preeclampsia and its adverse neonatal consequences, and measures should be taken to promote the health of newborns in the community.

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Declarations

Conflicts of interest The authors declared that they have no conflict of interest.

Ethical approval This study was approved by the Ethics Committee of Mashhad University of Medical Sciences (4001336- IR.MUMS.MEDICAL.REC.1400.770).

Research involving Human Participants and/or Animals Human participants.

Informed consent Informed consent was obtained from all individual participants included in the study.

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