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PERINATAL COMPLICATIONS OF PRETERM BABIES DELIVERED IN MALAYSIA'S TERTIARY HOSPITAL

** Malisa Kamaruzaman, ** Cheah Yun Tong, , *** Habibah Abdul Hamid, **** Maiza Tusimin, ***** Zulida Rejali, ****** Tan Niu Jin, ******* AmiliaAfzanMohd Jamil*

[*] Faculty of Medicine and Health Sciences, University Putra Malaysia [**] Medical Genetics Unit, Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia [***] Department of Obstetrics & Gynecology, Faculty of Medicine and Health Sciences, University Putra Malaysia

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Correspondence Author:
Amilia Afzanbinti Mohd Jamil
Department of Obstetric and Gynaecology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia 43400 UPM Serdang, Selangor DarulEhsan, MALAYSIA
Email: amilia@upm.edu.my

ABSTRACT

Background: The study on perinatal complications play a crucial role to guide clinicians in improving management of preterm babies especially to bring down the perinatal mortality rate, and to counsel patients with impeding premature delivery. **Aims & Objective:** To identify the perinatal complications of preterm babies born in a Malaysia's tertiary Hospital. **Methodology:** This cross-sectional study was conducted in one of Malaysia's tertiary hospital over 1 year period, involving 720 women delivered prematurely in the center. The individual preterm baby records was retrieved from computer database and data on gestational age, weight, dexamethasone prescription, mode of delivery and hx of premature prelabour rupture of membranes Preterm Prelabor Rupture of Membrane (PPROM). **Results:** Results display 55.1% male and 44.9% female born prematurely in the center. Among 720 preterm babies, 538 (74.7%) were Malays, 42 (5.8%) were Chinese, 36 (5.0%) were Indians and 104 (14.4%) were from other ethnicity. Majority of them (n=487 (67.6%) delivered vaginally. 29.2% babies born prematurely had at least one perinatal complications. Overall, perinatal complications are found to be significantly associated with gestational age, mode of delivery and birth weight. Prescription of dexamethasone is significantly associated with respiratory distress syndrome and intraventricular hemorrhage. Spontaneous preterm delivery only show significant association with intraventricular hemorrhage. Moreover, infants with gestational ages of less than 32 weeks and birth weight less than 1500g have higher risk to develop perinatal complications of respiratory distress syndrome, intraventricular hemorrhage and perinatal mortality. Apgar scores for Singleton preterm babies born with perinatal complications are significantly below normal when compared to singleton preterm babies born without perinatal complications. **Conclusion:** Majority of preterm babies delivered in the center for the year of 2015 were male, Malay and delivered vaginally. Vagina delivery reduces the risk of respiratory distress syndrome and perinatal mortality.

Keywords: preterm babies, perinatal complications, intraventricular hemorrhage, nectotizingenterocolitis, perinatal death, respiratory distress syndrome.

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INTRODUCTION

Morbidity and mortality of preterm babies are important issues in perinatal medicine, despite advancements in perinatal medicine and full-force preventive efforts by primary health care lines[1]. In managing these vulnerable babies, both obstetricians and neonatologist must be equipped with knowledge on likelihood of survival and the risk of complications premature neonates will face. This is important for patients' counselling and decision for early delivery, and to decide the best mode of delivery. Preterm babies are defined as the babies delivered between 22 to 37 completed weeks of gestation[2]. Preterm birth is sub-classified according to gestation at delivery into extreme preterm (less than 28 weeks), severe preterm (28 weeks to 31 weeks + 6 days), preterm (32 weeks to 33 weeks + 6 days) and near term (34 weeks to 36 weeks + 6)[3]. These infants may be born early precipitated by or as consequences of maternal problems, or spontaneously with no apparent precipitating factors. Preterm birth is the most common cause of neonatal death, with about 3.1 million babies per year dying as a direct result of preterm birth[2].

Complications of preterm babies are becoming more common as more survivors are spending time in newborn intensive care units (NICUs)[4]. Although with the advancement in neonatology, and better preventive measures in health care as well as tertiary center's setting, prematurity is still one of the leading cause of eminent mortality and neonatal morbidity. The struggle, therefore, remains a major concern, especially in developing countries, where modern neonatal intensive care techniques are not always available[5].

MATERIALS AND METHODS

A cross-sectional study utilizing pro forma was conducted in Hospital Serdang, Malaysia, a tertiary center situated in the Klang Valley where the number of deliveries reach up to 10,000 per year. This research was approved by the Ethic Committee for Research Involving Human Subject (Jawatan kuasa Etika Universiti Melibatkan Manusia, JKEUPM) and National Medical Research Register (NMRR).

This study involved preterm babies delivered in the center over one year period from 1 January 2015 until 31 December 2015. Preterm babies were identified using delivery registry books of Hospital Serdang. The individual preterm baby records were retrieved from the computer database while data on gestational age, weight, dexamethasone prescription, mode of delivery and preterm deliveries with intact or ruptured membrane were recorded. Gestational age was based on an assessment of last menstrual period (LMP) and earliest reliable ultrasound examination dating. We excluded preterm babies born from a mother who is unsure of the gestational age, multiple pregnancies, lethal congenital abnormalities and still birth. Sample size was calculated by using hypothesis testing proportion with value of confidence level at 95%, which gives the z value of 1.96. $Z_{1-\beta}$ stands for 20% beta error, therefore, 80% power; $z_{1-\beta}$ =0.84. Total of 720 preterm babies that have been reviewed for their sociodemographic which are gender and ethnicity, gestational age, weight, prescription of dexamethasone, modes of delivery and history of Preterm Prelabor Rupture of Membrane (PPROM) were recorded in proforma. Information collected in the proforma were entered and analyzed into master sheet using the Statistical Package for Social Science (SPSS) version 22. The perinatal complications tested included respiratory distress syndrome, necrotizing ecterocolitis, intraventricular hemorrhage and perinatal mortality.

Exclusion criteria: We excluded preterm babies born from a mother who is unsure of the gestational age, multiple pregnancies, lethal congenital abnormalities and still birth.

RESULTS

The study was conducted over 1 year period including deliveries which occurred between January 2015 and December 2015, involving 720 women who delivered singleton preterm babies. Majority of them were Malays, followed by Chinese and Indians. Most of these babies were male (55.1%), with 67.6% of them delivered vaginally (table 1.0).

210 (29.2%) of preterm singleton babies were born with at least one perinatal complication.Chi-square test of independence showed maternal age of more or less than 32 years old, premature babies born by cesarean deliveries (CD) , babies with low Apgar score (AS) and low birth weight (LBW) and extremely low

Table 1.0:
Sociodemographic Characteristics and mode of deliveries.

PretermBabies Characteristic	Frequency (n)	Percentage (%)
Gender		
Male	397	55.1
Female	323	44.9
Total	720	100.0
Ethnicity		
Malay	538	74.7
Chinese	42	5.8
Indian	36	5.0
Others	104	14.4
Total	720	100.0
Modes of Delivery		
Vagina	487	67.6
Caesarian	233	32.4
Total	720	100.0

birth weight (ELBW) were at significantly higher risk of at least one perinatal complications (Table 2.0).

There is a significant association between respiratory distress syndrome with EPT AND SPT, low birth weight (LBW) and extremely low birth weight (ELBW), dexamethasone administration and cesarean deliveries (CD) (Table 2.1). However there is no significant association of respiratory distress syndrome (RDS) with Premature Prelabour Rupture of Membranes (PPROM).

Our studies also demonstrated no significant association between necrotizing enterocolitis (NEC) and gestational age, birth weight of preterm babies, dexamethasone administration, modes of delivery and Preterm Prelabor Rupture of Membrane (PPROM), as shown in Table 2.2.

Interestingly, there are significant associations between intraventricular hemorrhage (IVH) and dexamethasone administration, along with gestational age at birth, birth weight of preterm babies and Preterm Prelabor Rupture of Membrane (PPROM) (Table 2.3).

There are also significant association between perinatal mortality with gestational age at delivery and birth weight, as well as cesarean deliveries (CD) and Preterm Prelabor Rupture of Membrane (PPROM).

In the final analysis, we can conclude that besides EPT and SPT, low birth weight (LBW) and extremely low birth weight (ELBW) also have significant associations with RDS, IVH and perinatal mortality but interestingly, dexamethasone prescription, which supposedly helps in reducing prematurity complications, is significantly associated with higher RDS and IVH in premature infants. cesarean deliveries (CD) was also significantly associated with RDS and perinatal mortalreas Preterm Prelabor Rupture of Membrane (PPROM) have significant association with IVH.

DISCUSSION

The incidence of preterm births in Hospital Serdang was 10.09%, which is higher compared to the incidence rate in North America, which was 7.4%[6]. Preterm birth is disproportionately concentrated in Africa and Asia (31% and 54%, respectively)[6]. Studies had revealed that incidence was higher in developing countries than in developed countries[7]. The reasons behind this are largely due to improvement in the quality of antenatal care services, as well as neonatal support for premature babies in a developed country. Interestingly, although Malaysia is considered a developing country, the incidence of preterm birth is almost comparable to developed countries, which shows that the government's effort to curb perinatal morbidities and mortalities by improving neonatal support, especially in tertiary referral center, is effective.

Table 2.0.
Univariate analysis of various factors associated with perinatal complications in singleton preterm birth.

Variables	Perinatal Complications		X^2	p-value
	Yes n (%)N= 210	No n (%)N= 510		
Ethnicity				
Malay	150 (27.9)	388 (72.1)	3.703	0.295
Chinese	16 (38.1)	26 (61.9)		
Indian	14 (38.9)	22 (61.1)		
Others	30 (28.8)	74 (71.2)		
Gestational aged				
”31 yearse	89 (80.9)	21 (19.1)	168.254	<0.0001*
”32 years	121 (19.8)	489 (80.2)		
Gender				
Male	105 (26.4)	292 (73.6)	3.165	0.075
Female	105 (32.5)	218 (67.5)		
Mode of				
Delivery	112 (23.0)	375 (77.0)	27.719	<0.0001*
Vaginal	98 (42.1)	135 (57.9)		
delivery				
Caesarean section				
Birth weight				
d”1.499kge	101 (81.5)	23 (18.5)	198.215	<0.0001*
”1.500kg	109 (18.3)	487 (81.7)		
1-min Apgar				
score	79 (84.9)	14 (15.1)	160.832	<0.0001*
<6	131 (20.9)	496 (79.1)		
>6				
5-min Apgar				
Score	57 (93.4)	4 (6.6)	133.275	<0.0001*
<6	153 (23.2)	506 (76.8)		
>6				
*Statistically significant				

Our study demonstrated that 29.2% of preterm singleton babies were born with at least one perinatal complication, namely RDS, NEC, IVH and perinatal mortality. These preterm babies were found to have lower Apgar score (AS) at both 1 and 5 minutes as compared to preterm babies born without any perinatal complication.

Respiratory distress syndrome (RDS) is defined as respiratory failure secondary to surfactant deficiency[8]. The occurrence of respiratory distress syndrome (RDS) in infants with gestational age of less than 32 weeks was 35.4% based on a study conducted by Khoshnood et al which was lower when compared with our finding, 50.9%[1]. According to Jakiel et al, there is no association between RDS and modes of delivery[9]. According to Deulofeut et al, there is an association between cesarean

Table 2.1:
Association of variables with respiratory distress syndrome

	Respiratory Distress Syndrome				X^2	p-value	OR
	YES n	%	NO n	%			
Gestational Age at delivery	4.93						
Extreme and Severe Preterm	56	50.9	54	49.1	60.093	Less than 0.001	
Preterm and Near Term	106	17.4	504	82.6			
Weight of Preterm Babies							
ELBW and VLBW	64	51.6	60	48.4	72.811	Less than 0.001	5.42
LBW and NBW	98	16.4	498	83.6			
Prescription of Dexamethasone	3.84						
YES	101	37.5	168	62.5	55.756	Less than 0.001	
NO	61	13.5	390	86.5			
Modes of Delivery							
Vaginal	71	14.6	416	85.4	54.147	Less than 0.001	
Caesarean	91	39.1	142	60.9			0.27
PPROM							
YES	31	20.4	121	79.6	0.490	0.514	0.85
NO	131	23.1	437	76.9			

LBW: Low Birth Weight
VLBW: Very Low Birth Weight
ELBW: Extremely Low Birth Weight
NBW : Normal Birth Weight
PPROM: Preterm Prelabor Rupture Of Membrane

deliveries and better neonates' perinatal result[10]. The delivery mode is considered responsible for higher occurrence of respiratory distress syndrome[5]. Our study, however, showed contrary results to the above mentioned studies, as there is a higher incidence of respiratory distress syndrome among neonates born by cesarean deliveries, 91 (39.1%) compared to only 71 (14.6%) of preterm babies delivered vaginally. Our result is supported by Anon et al study which concluded that neonates delivered by cesarean sections had a higher incidence of respiratory morbidities[11]. This was an expected outcome, considering that hormonal and physiological changes associated with labour are necessary for pulmonary maturation[11].

This study also demonstrated that there is a higher incidence of respiratory distress syndrome after the prescription of dexamethasone, despite the fact that dexamethasone usually helps to reduce the frequency and intensity of respiratory distress syndrome (RDS) in infants and other complications related to early delivery[9]. The significant association of antenatal steroid therapy and RDS in this study is more likely due to the practice of giving dexamethasone 12mg 12 hourly, instead of 6mg, 4 doses, 12 hours apart as recommended by NICE guidelines. However, further study needs to be done to look into the interval between dexamethasone

Table 2.2:
Association of variables with necrotizing enterocolitis

	Necrotizing Enterocolitis				X^2	p-value	OR
	YES n	%	NO n	%			
Gestational Ages							
Extreme and Severe Preterm	1	0.9	109	99.1	NA	0.153 (Fisher's Exact Test)	-
Preterm and Near Term	0	0.0	610	100			
Weight of Preterm Babies	-						
ELBW and VLBW	1	0.8	123	99.2	NA	0.172 (Fisher's Exact Test)	
LBW and NBW	0	0.0	596	100			
Prescription of Dexamethasone							
YES	1	0.4	268	99.6	NA	0.374 (Fisher's Exact Test)	-
NO	0	0.0	451	100			
Modes of Delivery							
Vaginal	0	0.0	487	100	NA	0.324 (Fisher's Exact Test)	
Caesarean	1	0.4	232	99.6			-
PPROM							
YES(ruptured of membrane)	0	0.0	152	100	NA	1.000 (Fisher's Exact Test)	-
NO (intact of membrane)	1	0.2	567	99.8			

LBW: Low Birth Weight
VLBW: Very Low Birth Weight
ELBW: Extremely Low Birth Weight
NBW: Normal Birth Weight
PPROM: Preterm Prelabor Rupture Of Membrane

administration and deliveries, association between dexamethasone administration and complications in different categories of premature infants as well as exclusion of other factors contributing to respiratory morbidities such as sepsis.

Intraventricular Hemorrhage or bleeding into ventricles of the brain is higher in preterm babies with gestational age of less than 32 weeks. Our study showed IVH incidence of 5.5%, which is lower than the study by Khoshnood et al (9%)[1]. This again proves the fact that adequate and updated facilities in Malaysia's tertiary centers have helped reduce the morbidities in premature babies.

In our study, there is a significant association between the birth weight and IVH. The incidence of IVH in extremely low birth weight (ELBW) (<1000g) and Very Low Birth Weight (VLBW) (1000-1499g) of 7 (5.6%) is higher comparable to only 3 (0.5%) in

Table 2.3:
Association of variables with intraventricular hemorrhage

	Intraventricular Hemorrhage				X^2	p-value	OR
	YES n	NO %	n	%			
Gestational Ages Extreme and Severe Preterm	8.74 6	5.5	104	94.5	NA	0.001 (Fisher's Exact Test)	
Preterm and Near Term Weight of Preterm Babies ELBW and VLBW	4 7	0.7 5.6	606 117	99.3 94.4	NA	Less than 0.001 (Fisher's Exact Test)	
LBW and NBW Prescription of Dexamethasone YES	3 7	0.5 2.6	593 262	99.5 97.4	NA	0.046 (Fisher's Exact Test)	11.83 3.99
NO Modes of Delivery Vaginal	3 5	0.7 1.0	448 482	99.3 99.0	NA	0.306 (Fisher's Exact Test)	
Caesarean PPROM YES	5 5	2.1 3.3	228 147	97.9 96.7	NA	0.040 (Fisher's Exact Test)	0.47 3.83
NO	5	0.9	563	99.1			

LBW: Low Birth Weight
VLBW: Very Low Birth Weight
ELBW: Extremely Low Birth Weight
NBW : Normal Birth Weight
PPROM: Preterm Prelabor Rupture Of Membrane

low birth weight (LBW) (1500-2499g) and Normal Birth Weight (NBW) (≥2500g). This is in accordance to a study by Anon et al, in which neonates weighing < 1500g were shown to have higher incidence of IVH compared to neonates weighing >1500g[10]. The occurrence of intracranial hemorrhage seems to be caused by the immaturity of cerebral flow self-regulation and to the fragility of the vascular bed matrix, which is more likely to happen in low gestational age and low birth weight preterm babies, although the role of trauma could not be excluded[11].

According to a research conducted by Mentet. al in 2005, no antenatal steroid treatment (19% vs 32%, p = 0.03) and vaginal deliveries (71% vs 45%, p <

Table 2.4:
Association of variables with perinatal mortality

	Perinatal Mortality				X^2	p-value	OR
	YES n	NO %	n	%			
Gestational Ages							
Extreme and Severe Preterm	37	33.6	73	66.4	135.193	>0.001	20.11
Preterm and Near Term	15	2.5	595	97.5			
Weight of Preterm Babies							
ELBW and VLBW	42	33.9	82	66.1	158.762	>0.001	
LBW and NBW	10	1.7	586	98.3			30.01
Prescription of Dexamethasone							
YES	14	5.2	255	94.8	2.609	0.136	
NO	38	8.4	413	91.6			0.6
Modes of Delivery							
Vaginal	42	8.6	445	91.4	4.415	0.044	
Caesarean	10	4.3	223	95.7			2.1
PPROM							
YES	8	5.3	144	94.7	1.104	0.378	0.66
NO	44	7.7	524	92.3			

LBW: Low Birth Weight
VLBW: Very Low Birth Weight
ELBW: Extremely Low Birth Weight
NBW : Normal Birth Weight
PPROM: Preterm Prelabor Rupture Of Membrane

0.0001) were associated with lower risk of IVH[12]. In our study, there were more preterm babies born from mother that was given dexamethasone, which had IVH (2.6% vs 0.7%). Preterm babies born via cesarean sections also had higher incidence of IVH compared to vaginal delivery (2.1% vs1.0%), although not statistically significant. Hanke et al proved that there was no significant association between Preterm Prelabor Rupture of Membrane (PPROM) and IVH[13]. This supports our findings of no significant association between Preterm Prelabor Rupture of Membrane (PPROM) and IVH as well, although the incidence of IVH seems to be higher in Preterm Prelabor Rupture of Membrane (PPROM) group (3.3% vs 0.9%). Although sepsis is highly associated with development of IVH, proper antenatal management with antibiotics in mothers with Preterm Prelabor Rupture of Membrane (PPROM), as well as administration of antibiotics in high-risk babies reduces the risk of sepsis, hence improves the outcome of premature babies.

The perinatal mortality rate for premature infants born at less than 32 weeks was reported at 15% in Khoshnoodet. al study[1], which is almost similar to the study by Larroque et al (14%) and Torres et al (16%)[14,15]. However, the perinatal mortality rate for infants with gestational age less than 32 weeks was 33.6% in our study, which is surprisingly higher as compared to the mentioned studies. However, this study does not necessarily represent the entire Malaysian population, and further study may need to be conducted.

Our study showed no significant association between perinatal mortality and Preterm Prelabor Rupture of

Membrane (PPROM) (5.3%), which was comparable with the findings by Martinet al[17].

Necrotizing enterocolitis is a universal complication in preterm infant. It is seen almost exclusively in preterm infants[2], and occurs 100 times more frequently in preterm instead of in term neonates[4]. The prevalence of necrotizing enterocolitis was 2.02% among infants born with gestational age less than 32 weeks and 1.3% among babies born at 32 weeks and 6 days respectively[1]. The severity and age of onset of NEC increase with decreasing birthweight and greater degrees of immaturity, frequently at 2-3 weeks after birth for infants with gestational ages of 32 weeks or less[4]. In a study reported by Negrini et al in 2015, the incidence of Necrotizing Enterocolitis was higher among neonates born by cesarean deliveries (CD) in all weight group, reinforcing the better results seen in VD[11]. Unfortunately, these findings contradicted to our study, which has shown no significant association of NEC with all the variables of interest. The adverse finding might be due to unfamiliarity of the perinatal complications for preterm infants in Hospital Serdang, and maybe because the study was confined to Hospital Serdang only and did represent the entire community.

CONCLUSION

For primary health care as well as obstetricians and neonatologist, not to forget the policy makers to play their role in preventing premature deliveries, as well as preventing the complications of premature infants, by providing adequate primary preventive measures in terms of modifying the modifiable risk factors, avoiding unnecessary iatrogenic premature deliveries, and increased resources, in particular neonatal support to meet the needs for care of this high risk preterm babies.

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DECLARATION

We declare that the project is our original work except for quotations and citations which have been duly acknowledged. We also declare that it has not been previously and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institutions.

Authors contribution:
All authors equal contributions.

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