

## Antenatal parameters to predict mortality and major morbidity in very low birth weight preterm neonates

Ghanshyam Das<sup>1</sup>, Shweta Gautam<sup>2</sup>

From <sup>1</sup>Professor, <sup>2</sup>Senior Resident, Department of Pediatrics, G R Medical College, Gwalior, Madhya Pradesh, India

**Correspondence to:** Dr. Shweta Gautam, Department of Pediatrics, G R Medical College, Hospital Road, Gwalior, Madhya Pradesh - 474 009, India. E-mail: shwetagautam1512@gmail.com

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### ABSTRACT

**Objectives:** The objective of this study was to determine effect of maternal factors and abnormal antenatal color Doppler of umbilical artery on mortality and major morbidity in very low birth weight (VLBW) neonates. **Materials and Methods:** This prospective study was conducted in the Department of Pediatrics, of a teaching institution of central India. All consecutive intramural live-born preterm neonates, delivered with BW of 1000–<1500 g, were included in the study. All preterm neonates received standardized neonatal care as per the unit protocol. A total of 400 intramural live-born VLBW, preterm neonates (diagnosed as per WHO criteria) were included in the study; out of which, 103 had absent or reversed end-diastolic blood flow and 117 had forward end-diastolic blood flow and in the remaining 180 babies, color Doppler could not be done. All the VLBW neonates were followed up till the time of discharge or death. The mortality and major morbidity (one or more of the following: intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC) during hospital stay were assessed in all the babies. **Results:** A total of 400 preterm neonates were enrolled in study, out of which, 109 died (27.25%). The causes of neonatal mortality included septicemia (44.9%), birth asphyxia (18.34%), hyaline membrane disease (30.6%), pulmonary hemorrhage (11.34%), prematurity (10.09%), aspiration pneumonia (8.25%), IVH (1.83%), and NEC (1.83%). Abnormal antenatal Doppler 15.1 (8.7–25.5) ( $p=0.0001$ ) was an important factor for the major morbidities. Among maternal risk factors, premature rupture of membrane ( $p=0.015$ ), meconium-stained liquor ( $p=0.01$ ), fetal distress ( $p=0.001$ ), and the absence of antenatal steroid ( $p=0.0001$ ) significantly predict the mortality. **Conclusion:** Among maternal factors, premature rupture of membrane, meconium-stained liquor, and abnormal antenatal color Doppler are the important predictors of early mortality and major morbidities such as respiratory distress syndrome, IVH, NEC in VLBW neonates

**Key words:** Absent or reversed end-diastolic blood flow, Forward end-diastolic blood flow, Mortality, Very low birth weight

Very low birth weight (VLBW) is defined as BW <1500 g at birth irrespective of gestational age [1]. BW and GA are two of the most important factors that predict the short- and long-term quality of life of neonates. Low BW and GA are linked to morbidity and mortality during the newborn period [1-5]. Premature births result in newborn mortality and morbidity rates of 70% and 75%, respectively [6]. Hence, there has been an effort in recent times to define physiological and laboratory parameters which would be predictive of neonatal mortality. The immature biological and physiological characteristics of these premature infants often lead to pathologies, such as respiratory distress syndrome (RDS), symptomatic patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC), retinopathy of prematurity, intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), and bronchopulmonary dysplasia (BPD), which affect prognosis. Moreover, these infants are also deemed to be a high-risk group for poor neurodevelopmental outcome [7].

Advanced technology in Neonatal Intensive Care Unit (NICU) facilities, the availability of sophisticated and experienced NICU staff, appropriate use of mechanical ventilation, surfactant

therapy, and the advent of antenatal and postnatal corticosteroid treatments have increased the survival rates of VLBW neonates up to 95% [8]. However, the elevated survival rates have also elicited an increase in morbidity rates.

The major predictors for this are maternal factors (maternal medical illness, significant obstetric problems, and use of antenatal steroids), BW, GA, Apgar scores, RDS, acid-base status, laboratory parameters, and imaging [2]. In the present study, we aimed to determine the mortality and morbidity rates of VLBW infants admitted to a NICU and to define associated antenatal risk factors.

### METHODS

The study was conducted at Department of Pediatrics, of a teaching institution in Central India after getting approval from the Institutional Ethical Committee and written consent from parents or legal guardians. 400 intramural live-born preterm VLBW neonates (diagnosed as per WHO criteria) were included in the study. Neonates with lethal congenital malformations,

intrauterine growth retardation, GA <26 weeks and neonates who died in delivery room were excluded from the study.

All neonates received standardized neonatal care as per protocol both at birth in NICU. The data were prospectively recorded in all VLBW neonates at birth and at the time of admission to NICU and following information were noted: BW, sex, Apgar scores at 1 and 5 min, assisted ventilation at the time of birth, need for and duration of resuscitation at birth, presence of significant maternal illnesses (e.g., pregnancy-induced hypertension, eclampsia, maternal fever), presence of significant obstetric problems (e.g., prolonged rupture of membranes (PROM), meconium-stained amniotic fluid [MSAF], and fetal distress), and absent use of antenatal steroid.

Vitals (heart rate, respiratory rate, capillary filling time >3 s, temperature, and urine output) were noted. The enteral feeding was initiated within 3 days in hemodynamically stable neonates. Clinical evidence of PDA and clinical and radiological evidence of RDS and NEC were documented. Ultrasound scan evidence of IVH and BPD was also documented. BPD was defined as persistent oxygen requirement at 28 days of life. NEC was diagnosed when there was abdominal distension with bile-stained gastric aspirate or nausea in a sick baby, who might have had bloody mucous stools, thrombocytopenia, and coagulopathy with radiological findings of reduced bowel gas shadowing, thickening of bowel wall, and pneumatosis coli. All the neonates were studied until the time of discharge or death. Outcome was assessed in terms of the mortality and major morbidity (one or more of the following: IVH and NEC) during hospital stay.

## RESULTS

A total of 400 subjects were enrolled into the study; out of which, 103 neonates had abnormal or reversed end-diastolic arterial blood flow (AREDF), and 117 had forward end-diastolic blood flow and in the remaining 180 babies, color Doppler could not be done. Out of 400 neonates, 109 neonates died (27.25%). The causes of neonatal mortality were septicemia (44.9%), birth asphyxia (18.34%), HND (30.6%), pulmonary hemorrhage (11.34%), prematurity (10.09%), aspiration pneumonia (8.25%), IVH (1.83%), and NEC (1.83%) as shown in Table 1.

Low BW and GA were significantly associated with mortality ( $p < 0.005$ ). Abnormal cranial ultrasonography (12.2 [7.2–20.5],  $p = 0.001$ ), abnormal color Doppler (15.1 [8.7–25.5],  $p = 0.0001$ ), supplementary oxygen ( $p = 0.0001$ ), ventilator support ( $p = 0.0001$ ), and requirement of assisted ventilation at the time of birth ( $p = 0.001$ ) were the predictors of major mortality.

Initiation of enteral feeding within 3 days significantly lowers the neonatal mortality in VLBW neonates ( $p = 0.035$ ) (Table 2). Among maternal risk factors, PROM ( $p = 0.015$ ), MSAF ( $p = 0.01$ ), fetal distress ( $p = 0.001$ ), and absence of antenatal steroid ( $p = 0.0001$ ) were the significant predictors of the mortality (Table 3).

## DISCUSSION

This study was conducted to evaluate the predictors of neonatal mortality and major morbidities. Great care was taken in the

**Table 1: Primary causes of neonatal mortality**

Primary causes of mortality	Neonatal mortality (n=109)	
	n (%)	
Septicemia	49	(44)
Birth asphyxia	20	(18)
Hyaline membrane disease	12	(11)
Prematurity	11	(10)
Aspiration pneumonia	09	(8)
Pulmonary hemorrhage	04	(4)
Intraventricular hemorrhage	02	(1.8)
Necrotizing enterocolitis	02	(1.8)

**Table 2: Significant factors associated with neonatal mortality**

Variable (n)	Alive (291), %	Death (109), %	p value
Gestational age <30 week (117)	15	45	0.001
Birth weight <1.2 kg (97)	15	48	0.001
Meconium-stained liquor (91)	21	58	0.001
Fetal distress (86)	10	33	0.001
Enteral feeding after 3 days (203)	52	75	0.035
Abnormal cranial USG (140)	20	64	0.0001
Abnormal color Doppler (101)	11	70	0.001
Supplementary oxygen (125)	17	55	0.0001

USG: Ultrasonography

**Table 3: Maternal risk factors as predictors of mortality**

Maternal risk factors (n)	Survived (291), %	Death (109), %	p value
PIH (95)	24.74	21.10	0.44
Eclampsia (85)	19.93	24.77	0.29
Maternal fever (46)	6.87	23.05	0.101
Premature rupture of membrane (98)	21.30	33.02	0.015
MSAF (91)	21.30	26.60	0.001
Fetal distress (86)	21.64	21.10	0.001

PIH: Pregnancy-induced hypertension, MSAF: Meconium-stained amniotic fluid

methodology to ensure accuracy and reproducibility of the observations. In this study, apart from sepsis (43%), HMD (11%), and prematurity (10%) were the common causes of neonatal mortality. Less common causes were pulmonary hemorrhage, IVH, and NEC. We found that abnormal antenatal Doppler was significantly associated with neonatal mortality and early brain injury, RDS, and PVL as shown in a previous study by Maunu *et al.* [6]. We also found that the absence of antenatal steroid was significantly associated with neonatal mortality. The use of antenatal steroid has shown to significantly reduce the neonatal mortality by reducing RDS, IVH, and NEC by many previous studies also [7-11].

Absent end-diastolic flow velocity in the fetal umbilical artery or aorta has been shown to be associated with high mortality [12,13], increased risk of NEC [12-14], and hemorrhage [12]. Our results were in favor of these findings as there was an association of AREFD with the increased incidences of NEC, IVH, pulmonary hemorrhage, or neonatal death. The cause of NEC is multifactorial and its frequency varies between centers [15], and in addition, AREFD indicates a fetus under vascular stress, and delivery at different points in the deteriorating fetal environment was a major factor for change in the results. Our results were similar to the findings of McDonnell *et al.*, [16] in which seven of the 61 babies with AREFD velocities had NEC compared to only one of the controls, although the difference was not statistically different. In keeping with our findings, they did not show an association with increased neonatal morbidity and mortality.

In our study, there was higher incidence of RDS among the babies with AREFD, and the difference was significant. Fetuses with acute or chronic intrauterine hypoxia may mount up a mechanism which results in absent end-diastolic flow velocity. The persistence of this insult might reverse the end-diastolic flow. When this compensatory mechanism is overwhelmed, the fetus could present with fetal compromise, as shown by poor biophysical profile and/or abnormal cardiotocography. If the fetus will not be delivered then, there could be an intrauterine death.

## CONCLUSION

Among maternal factors, early rupture of membrane, MSAF, and abnormal antenatal color Doppler are the important predictors of early mortality and the major morbidities in preterm, VLBW neonates.

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