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Original Research Article

Study of variables affecting mortality among extramural very low birth weight neonates in tertiary care centre: a prospective observational study

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ABSTRACT

Background: Over the past few decades, the burden of extramural very low birth weight (VLBW) neonates is increasing due to advances in obstetrics services. Objective of present study was to know variables affecting mortality in these neonates.
Methods: A prospective observational study was conducted at department of paediatrics, government medical college and hospital, Nagpur, India over a period of 2 years. Out-born neonates admitted in this tertiary care centre with birth weight between 1000-1499 gm were included in the study. Proper antenatal, natal history were taken and data was collected using data collection sheet. All subjects were followed up till discharge or death whichever was earlier.
Results: Significant demographic factors associated with neonatal mortality were found out to be place of birth, birth attendant, distance travelled and transport time. Neonatal factors which significantly associated with mortality were found out to be hypothermia and SpO_2 less than 90%.
Conclusions: Univariate analysis concluded that age at presentation (>24 hours), place of birth, birth attendant, distance travelled, mode of transport, transport time, hypothermia, SpO_2<90% were found to be significant factors for predicting risk of mortality in VLBW neonates. However, multivariate analysis concluded only 4 predictors that is age more than 24 hours, transportation time, SpO_2 on admission and hypothermia were found to retain their significance. VLBW babies are vulnerable, but with small improvements in infrastructure and personnel training, significance difference in prevention of morbidity and mortality can be seen.

Keywords: VLBW, Outborn, Mortality

INTRODUCTION

The major causes of newborn etiology in India are prematurity (35%), sepsis (33%), perinatal asphyxia (20%) and congenital malformations (9%). VLBW preterm infants' numbers are increasing over the past two decades due to new advances in obstetrical practice.[1] VLBW babies constitute approximately 4-7% of all live births but constitute a major share of effort, time and resources for their care.[2] The survival rate of VLBW infant in India is only about 63%.[3,4] Doubts are still there about risk factors which accompany VLBW deliveries and that may be critical in determining proportion of survivors. Prognosis depends not only on birth weight and gestational age but also on demographic factors, perinatal factors and physiological condition of infants.

Worldwide, the survival rate of VLBW infant ranges between 43% in developing countries to more than 90% in developed countries such as Netherlands. In India, it is about 63%. This gap in infant survival is due to poor coverage of health system, less number of health care providers, and limited access to referral services.[5] Survival of these babies is inversely associated with their

birth weight, gestation and illness severity. Care of VLBW newborn still remains challenge for paediatrician as these babies are at increased risk of developing neonatal complications and its long-term sequelae.

At the same time, facility of transport in India are not encouraging. Most of neonatal transports are self-transported without any stabilization during transport. Many of these new-borns transported are cyanosed and hypoglycemic and 75% of babies transferred this way have serious clinical implications.[6] Currently, there is limited or no dedicated neonatal transport service is available in India. At the same time, it is well known that transport of new-born by a skilled organised team reduces neonatal mortality. Thus, the purpose of this study was to determine the factors predictive of mortality in out-born VLBW neonates within the Indian settings.

METHODS

A prospective observational study conducted at department of paediatrics, Government Medical College and Hospital, Nagpur, India over a period of 2 years from October 2018 to October 2021. Out-born neonates admitted in this tertiary care centre with birth weight between 1000-1499 gm were included in study. Neonates with birth weight of more than 1500 gm and less than 1000 gm, those with congenital malformations, those not willing for participation and neonates discharged against medical advice (within 48 h of admission) were excluded from the study. After ethical clearance from institutional ethical committee, all out-born VLBW neonates who fulfilled inclusion criteria were enrolled. Proper antenatal and natal history were taken. Data was collected using structured data collection sheet. It included:

Birth data

Included birth weight, gender, gestational age (as per new Ballard score), cried immediately after birth/not, type of birth attendant (trained dai, ANM, medical officer).

Physiologic data

Physiologic data included temperature, heart rate, blood glucose, saturation and capillary refill time.

Demographic data

It included residence (rural or urban) and the place of birth (home or hospital).

Transport data

Distance from tertiary care centre (<50 km, 50-100 km, >100 km), mode of transport (ambulance with or without health assistant, private vehicle), transport duration (<1 hour, 1-3 hours, >3 hours) included int this data.

Pre-arrival data

The age in hours and duration of hospital stay recorded in pre arrival data.

Postnatal data

Acute life-threatening events like cyanosis, jaundice, respiratory distress, hypothermia, convulsions and apnoea were recorded.

Laboratory data

Lab data collected were complete haemogram, sepsis screen, blood/CSF culture, renal function test, serum biochemistry.

Others

Provisional diagnosis and outcome (discharge or death) data also were collected.

Major morbidity and major cause of death were also noted down. The outcome measure was in-hospital death. All subjects were followed up till discharge or death whichever was earlier.

Statistical analysis

Considering the expected proportion of mortality in VLBW neonates in a tertiary care hospital be 40.8%, with relative precision of 15%, considering desired confidence level (1-α) being 95%, the minimum sample size was found to be 150. Continuous variables (demographic and hemodynamic parameters) were presented as Mean ± SD. Categorical variables were expressed in frequency and percentages. Continuous variables were compared between survivors and deaths performing independent t test for normalized data and for non-normalized data, Mann-Whitney test. Categorical variables were compared between survivors and deaths by performing chi-square test. For small numbers, Fisher exact test was used wherever applicable. Odds ratio, 95% confidence interval were calculated to find association of different factors with deaths. Multivariate logistic regression was performed to determine independent predictors of deaths in patients of extra mural VLBW in neonates. $P<0.05$ was considered as statistical significance. Statistical software STATA version 14.0 was used for statistical analysis.

RESULTS

Out of total 150 subjects enrolled in this study, 97 survived, 53 died. Overall case fatality rate came out to be 35.33% while survival rate came out to be 64.67%. Out of 53 neonates in non-survivor group, there were 12 cases of age less than 24 hours, 18 cases of 24 to 71 hours of age, 16 cases of 72 to 120 hours of age and 7 cases of more than 120 hours of age. In survived group out of 97 neonates, 48 cases of less than 24 hours of age, 35 cases

of 24 to 71 hours of age, 10 cases of 72 to 120 hours of age and 4 cases of more than 120 hours of age. It was found that there was significant difference in age-wise distribution between non survivor and survived group (p<0.001), suggesting that neonates admitted at age of more than 120 hours of age had high mortality (Table 1).

Out of 53 neonates in non-survivor group, there were 30 males (56.60%) and 23 females (43.39%). In survived group out of 97 neonates, 60 (61.85%) were males and 37 (38.14%) females. It was found that there no significant difference in gender distribution between non survivor and survivor group (p=0.530), suggesting gender was not an important contributor to mortality risk for extramural VLBW neonates (Table 2).

Demographic factors

Univariate analysis of demographic factors revealed that birth attendant, place of birth, mode of transport as ambulance without health assistant, mode of the transport with the health assistant, distance travelled, transport duration were significantly associated with mortality in extramural VLBW neonates with p=0.007, 0.018, 0.005, 0.027, 0.003 and 0.01 respectively. While, residence and mode of transport as private vehicle were not associated with mortality in this particular population (Table 3).

Neonatal factors

Univariate analysis of various neonatal factors revealed that hypothermia and saturation less than 90% were significantly associated with mortality in this population with p=0.0001 and 0.041 respectively. Others factors such as hypoglycemia. Delayed capillary refill time, gestational age, cry status after birth, were not associated with mortality (Table 4).

Multiple logistic regression analysis as shown in Table 5 revealed that age more than 72 hours on admission, hypothermia, transportation time and SpO_2 on admission were highly significant as independent predictor with p<0.0001, 0.001, 0.045 and 0.032 respectively.

Table 1: Association of age with outcome.

Age (hours)	Total cases	Survivors		Non-survivors		P value
		N	%	N	%	
≤24	60	48	80	12	20	Chi^2=17.88, p<0.001, HS
24-72	53	35	66.04	18	33.96	
72-120	26	10	38.46	16	61.54	
>120	11	4	36.36	7	63.64	

Table 2: Association of gender with outcome.

Gender	Total cases	Survivors		Non-survivors		P value
		N	%	N	%	
Male	90	60	66.67	30	33.33	Chi^2=0.3939 p=0.530, NS
Female	60	37	61.67	23	38.33	

Table 3: Association of demographic factors with outcome.

Factors		Total cases	Survivors		Non-survivors		P value
			N	%	N	%	
Residence	Rural	120	76	63.33	44	36.67	0.494, NS
	Urban	30	21	70.0	9	30	
Place of birth	Home	3	0	0	3	100	0.018, S
	Hospital	147	97	65.99	50	34.01	
Delivery attended	Trained dai	4	0	0	4	100	0.007, HS
	ANM	31	17	54.84	14	45.16	
	Medical officer	115	80	69.57	35	30.43	
Distance travelled (km)	<50	49	36	73.47	13	26.53	0.005, HS
	50-100	55	40	72.73	15	27.27	
	>100	46	21	45.65	25	54.35	
Mode of transport	Ambulance	59	34	57.63	25	42.37	0.005, HS
	Ambulance with health assistant	76	56	73.68	20	26.32	0.027, S
	Private	15	7	46.67	8	53.33	0.124, NS
Transport time (hours)	<1	49	38	77.55	11	22.45	0.010, S
	1-3	57	38	66.67	19	33.33	
	>3	44	21	47.73	23	52.27	

Table 4: Association of neonatal factors with outcome.

Factors		Total cases	Survivors		Non-survivors		P value
			N	%	N	%	
Gestational age (weeks)	Pre term	131	83	63.36	48	36.64	0.672, NS
	Term	16	11	68.75	5	31.23	
	Post term	3	3	100	0	0	
Birth weight	<1250	53	32	60.38	21	39.62	0.417, NS
	1250-1499	97	65	67.01	32	32.99	
Baby cried immediately after birth	Yes	135	87	64.44	48	35.56	0.864, NS
	No	15	10	66.67	5	33.33	
SpO_2	<90	22	10	45.45	12	54.55	0.041, S
	≥90	128	87	67.97	41	32.02	
RBS on admission	>40	128	83	64.84	45	35.16	0.913, NS
	≤40	22	14	63.64	8	36.36	
Hypothermia	Yes	58	25	43.10	33	56.90	<0.0001, HS
	No	92	72	78.26	20	21.74	
CRT delayed	Yes	30	18	60.0	12	40.0	0.438, NS
	No	120	81	67.50	39	32.50	

Table 5: Multiple logistic regression analysis showing predictors of mortality in extramural very low birth neonates.

Predictor	Adjusted odds ratio	96% confidence interval	P value
Age >72 (hours)	5.40	2.19-13.32	<0.0001, HS
Transportation time	2.40	1.01-9.56	0.045, S
SpO_2	3.25	1.10-9.56	0.032, S
Hypothermia	3.76	1.66-8.53	0.001, HS

DISCUSSION

The mortality rates of VLBW babies referred to tertiary care centre in India is quite higher than the developing world. This situation is mainly due to the poor infrastructure and limited resources for care during transport. There is an absence of data to explain the way in which birth weight, gestational age and transport risks interact to lead neonatal mortality in high mortality burden setting. The purpose of this prediction model study is to identify predictors of mortality in extramural VLBW neonates.

Present study reported case fatality rate of 35.33% which is significantly higher than the similar study done by Sachan et al.[7] High admission rate and lower doctor to patient ratio in our setup may be the cause of high mortality in our study. This study reveals that gestational age is not a significant predictor of mortality in extramural VLBW neonates. In present study, males were 60% and female were 40%, that is, there was slight male preponderance. However, the gender distribution between expired and survival group was not statistically significant. This is similar to observations made by Sachan et al.[7] There is significant difference in age wise distribution between non survivor and survived group (p<0.001), suggesting that neonates admitted at age of more than 120 hours of age have higher mortality. Similar findings were made in study by Verma et al.[8]

Present study suggests that residence of neonate is not significant predictor of mortality in extramural VLBW neonates with p=0.494. Present study suggests that, place of birth is a significant predictor of mortality in extramural VLBW neonates with p=0.018. Similar finding was reported by Sachan et al.[7] Present study suggests that type of birth attendant is a significant predictor of mortality in extramural VLBW neonates with p=0.007. Similar findings were noted by study done by Meshram et al.[9] Present study suggesting that travelling distance from birth place to tertiary centre is a significant predictor of mortality in extramural VLBW neonates with p=0.005. Similar finding was seen in the study done by Verma et al.[8] Longer the distance, more time is required for these referred VLBW neonates to reach higher centre. Also, care of temperature, oxygen saturation, euglycemia is difficult in the currently available transport resources. Therefore, higher mortality was found in these neonates. Present study suggests that mode of transport of neonate is a significant predictor of mortality in extramural VLBW neonates with p=0.005. Similar finding was reported by Verma et al.[8] Trained personnel for transport are able to take better care of temperature, maintain oxygen saturation or even do resuscitation if required. Therefore, favourable outcome was seen when these extramural VLBW neonates were accompanied by trained personnel. Present study suggests that transport time from birth place to tertiary centre is a significant predictor of mortality in extramural VLBW neonates with p=0.01. Similar to the study conducted by Sachan et al it

was found that transport time is a significant predictor of mortality in these neonates with p=0.0001.[7] Present study reported that neonates with birth asphyxia is not significant predictor of mortality in extramural VLBW neonates (p=0.864). Similar finding was seen in the study done by Buch et al.[6] Present study suggests that neonates having hypoglycemia on admission is not significant predictor of mortality in extramural VLBW neonates (p=0.913). Similar finding was seen in the study done be Pankaj et al.[6] This study suggests that presence of hypothermia is significant predictor of mortality in VLBW neonates with p=0.0001. Similar finding was noted in the study done by Buch et al.[6] Present study reported that neonates having SpO_2< 90% at admission is significant predictor of mortality in extramural VLBW neonates with p=0.041. Similar finding was reported in the study done by Sachan et al.[7] Present study suggests that presence of poor peripheral perfusion on admission is not found as significant factor for predicting risk of mortality in VLBW neonates (p=0.438). Similar finding was reported in the study done by Meshram et al.[9]

Also, multiple logistic regression analysis was performed to find predictors of mortality in extramural low birth neonates adjusting for role of other variables revealed that 4 predictors that is age more than 24 hours, transportation time, SpO_2 on admission and hypothermia were found to retain their significant contribution in predicting risk of mortality in extramural very low birth neonates.

Referral of the neonates with inadequate data such as significant antenatal and natal history and documentation of life-threatening events of neonates like seizures, hypo-glycemia, hypothermia, history of bleeding for disseminated intravascular coagulation and lack of investigation reports and course of the neonates in referring hospital make it difficult to give proper management to these referred neonates. In the case of VLBW new-borns, the study of factors associated with death will lead to the critical analysis of health care services and define actions aimed at improving care for this group. The study may lead to identify the different health care needs and provide infrastructure and facilities for intervention aimed at reducing infant death in VLBW neonates.

Limitations

Firstly, we lacked sufficient antenatal and natal data. We did not include data about the important antenatal and natal events of the baby, because of unavailability and unreliability of antenatal and natal data provided with referred mothers in our institute. Since, maternal morbidities such as eclampsia or gestational diabetes mellitus and Natal events such as APGAR score may have significant impact on neonatal mortality in preterm, ignoring this data may have had significant impact on our results.

We did not include severity scoring in our study because calculation of the scores needs estimation of fractional inspired oxygen (FiO_2), arterial blood gas analysis and monitoring of vitals including blood pressure but the ABG analysis was not possible for all subjects at our facility.

Also, the geographical dimensions of India and the diversity of social and cultural characteristics in different states of country, justify the need to conduct some larger studies and also more regional studies, so that more accurate knowledge of the Indian reality may come up.

CONCLUSION

Univariate analysis concluded that age at presentation (>24 hours), place of birth, birth attendant, distance travelled, mode of transport, transport time, hypothermia, SpO_2<90% were found to be significant factors for predicting risk of mortality in VLBW neonates. However, multivariate analysis concluded only 4 predictors that is age more than 24 hours, transportation time, SpO_2 on admission and hypothermia were found to retain their significance. We found that delivery at home and by inexperienced hands has higher mortality risk. It can be concluded that early identification of high-risk mother and early referral for baby to get delivered in centres with better infrastructure and by trained personnel is important in reducing morbidity and mortality in these neonates. Also, age of presentation of more than 24 hours has impact on mortality. So, early identification of these high-risk neonates is found to be important in decreasing mortality. More the distance travelled by neonates, transport through private vehicle and more the transport time, more is the mortality risk. So, creating the infrastructure closer to referral centre can decrease mortality in these neonates. Among the neonatal factors, hypothermia and cyanosis were found to be important predictors of mortality. The basic training to trained dais specifically for VLBW babies like maintenance of temperature, resuscitation if required and neonatal care during transport should be given. Transport with trained health care personnel, equipped with oxygen therapy, temperature maintenance, iv fluids and asepsis during transport may reduce the morbidity and mortality. Proper documentation of antenatal, natal history and significant postnatal events if any on referral notes can reduce morbidity and mortality in these neonates. Thus, the present study concludes that the morbidity and mortality in VLBW babies who are referred to higher centre can be reduced to larger extent. VLBW babies are vulnerable, but with small improvements in infrastructure and personnel training, significance difference in prevention of morbidity and mortality can be seen.

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