

Risk Factors, Complications and Immediate Outcome of Very Low Birth Weight Neonates in NICU, Tertiary Care Hospital

Dr. Nazma Parvin Shammy^{1*}, Dr. Md. Nurul Hossain², Dr. Reema Afroza Alia³¹Assistant Professor, Department of Pediatrics, Uttara Adhunik Medical College & Hospital, Dhaka, Bangladesh, **ORCID ID:** <http://orcidid.org/0000-0002-8863-9890>²Professor and Head, Department of Paediatrics, Uttara Adhunik Medical College & Hospital, Uttara, Dhaka, Bangladesh, **ORCID ID:** <http://orcidid.org/0000-0002-8863-9890>³Associate Professor, Department of Pediatrics, Uttara Adhunik Medical College & Hospital, Dhaka, Bangladesh, **ORCID ID:** <http://orcidid.org/0000-0002-7793-2143>DOI: [10.36347/sjams.2022.v10i09.011](https://doi.org/10.36347/sjams.2022.v10i09.011)

| Received: 11.06.2022 | Accepted: 03.07.2022 | Published: 10.09.2022

*Corresponding author: Dr. Nazma Parvin Shammy

Assistant Professor, Department of Pediatrics, Uttara Adhunik Medical College & Hospital, Dhaka, Bangladesh

Abstract

Original Research Article

Introduction: Last two decades have witnessed a steady improvement in the quality of perinatal care in Bangladesh. Around 4-8% of all live births are very low birth weight (VLBW) & low birth weight (LBW) is 10.6%. The present study was done to determine risk factors, complications, and immediate outcomes in VLBW babies. **Aim of the study:** The study aimed to find out the Risk Factors, Complications, and Immediate Outcomes of Very Low Birth Weight Neonates in NICU, Tertiary Care Hospital. **Methods:** A prospective observational study was conducted in the NICU of Tertiary Care Hospital, Dhaka, Bangladesh. A total of 162 low birth weight neonates (birth weight <1500 g) were assessed for the study from January 2020 to December 2020. The American Academy of Pediatrics protocol for neonatal resuscitation was followed for the management of VLBW. Data were entered in predetermined proforma and statistical analysis was done. **Result:** A total of 162 patients were enrolled and analyzed in this study. The study was done into two groups; 1st is Appropriate for Gestational Age (AGA) and 2nd is Small for Gestational Age (SGA). The relational outcome with antenatal steroids of the study. The antenatal steroid proportion is divided into given (N=69) and not given (N=93), the p-value of the incidence is 0.51 for RDS, 0.17 for NEC and 0.54 for IVH which are not significant. The last table of the result is describing the relative risk of complications in AGA and SGA babies; from the outcomes, 127 babies survived and 35 babies expired and the p-value was 0.059 which was a significant change. **Conclusion:** Appropriate birth weight, gestational age, female sex, and antenatal steroids improved survival amongst babies. Antenatal steroids reduced the incidence of RDS, NEC, and IVH when preterm delivery was inevitable. **Keywords:** Risk factors, Immediate outcome, Very Low birth weight, Neonates, NICU.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Very low birth weight is the condition where the weight of the newborn is less than 1500gm as against the normal weight at term between 2500gm and 4000gm. Around 4-8% of all live births are very low birth weight (VLBW) infants [1]. Around one-third of neonatal deaths are witnessed in this group [2]. WHO estimates that globally about 25 million LBW babies were born each year, consisting of 17% of all live births, nearly 95% of them in developing countries [3]. In Bangladesh, VLBW infants made up 7%, low birth weight 10.6%, respectively, of the preterm births. Europe, where 6.2% of the births were preterm, had the lowest rate [4]. Bangladesh, VLBW infants made up 7% of the low-birth-weight total but accounted for a third of the infant's death [5]. The outcome of VLBW

babies is affected by prematurity as well as the presence of short-term morbidities such as RDS, Patent Ductus Arteriosus (PDA), sepsis, NEC, and Chronic Lung Disease (CLD). Intraventricular hemorrhage (IVH) remains associated with high morbidity and mortality. Identification and hence, efforts to modify the factors associated with these morbidities will influence the intact survival of VLBW babies [6]. In the past two decades, the field of neonatology has experienced significant progress in medical care and improvement in overall patient survival. Advancements in technology, greater use of antenatal steroids and neonatal surfactant replacement therapy, better regionalization of prenatal and high-risk neonatal care, and a more comprehensive understanding of the physiology of immature infants have all contributed to a dramatic increase in survival of

very preterm infants [7]. Although they represent a small percentage of overall births and Neonatal Intensive Care Unit (NICU) admissions, VLBW infants are often the most critically ill and at the highest risk for mortality and long-term morbidity of any NICU patient contributing disproportionately to overall hospital days and consuming a large percentage of NICU personnel time, effort and cost of care [8]. Prematurity and low birth weight are major factors for neonatal mortality especially VLBW. Hence this study has been undertaken with the aim and objective to determine risk factors, morbidity patterns, and outcomes of VLBW babies during their period of hospital stay, so that necessary steps can be taken to reduce NMR in this VLBW group and ultimately reach target NMR.

METHODOLOGY & MATERIALS

A prospective observational study was conducted in *attending the NICU in a Tertiary Care Hospital, Dhaka, Bangladesh*. A total of 162 low birth weight neonates (birth weight <1500 g) were assessed for the study from January 2020 to December 2020. All VLBW (<1500g) neonates admitted within 72 hours of birth in the NICU during the study period were enrolled in the study. Babies with birth weight <600 grams, with major congenital anomalies incompatible with life, were excluded. Cases were studied after taking informed consent from the parents. Gestational Age (GA) was obtained from the maternal last menstrual period and confirmed with a 1st-trimester ultrasound. Then they were classified into preterm (<37 weeks of GA), the term (37-42 weeks of GA), and postterm (>42 weeks of GA) [9-11]. Gestational maturity was assessed by New Ballard Score [12]. The birth weight was plotted on a fetal infant growth chart by Fenton TR (2003) to classify the babies into small for gestational age (SGA) (birth weight <10th percentile for GA) and Appropriate for Gestational Age (AGA) (birth weight between 10th-90th percentile for GA) [13]. Delivery details, birth weight, sex, ANC check-up doses of antenatal steroids were obtained from the delivery records. Maternal risk factors were assessed with proper history and evaluating previous medical records. Maternal BP 140/90 mm mercury was taken as hypertension. (Division of nutrition, National Centre for Chronic Disease Prevention and Health). Neonates with Respiratory Distress Syndrome (RDS) received early and Continuous Positive Airway Pressure (CPAP) or Mechanical Ventilation when needed. Enteral feeding was initiated at the earliest and transitioned to full feeds depending on tolerance. Morbidities like Respiratory Distress Syndrome (RDS), birth asphyxia (HIE), sepsis, jaundice intraventricular hemorrhages (IVH), necrotizing enter colitis (NEC), apnoea, pulmonary hemorrhage, PDA, were predefined. IVH was graded using Volpe's classification [14]. NEC was defined as per modified Bell's staging [15]. Packed red blood cell

transfusion was given when Hct was <35% in neonates with ventilator support, <30% in neonates with heart failure & required resp. support and <21% in asymptomatic neonates. VLBW babies who were Appropriate for Gestational Age (AGA) were compared with those born Small for Gestational Age (SGA) in terms of associated maternal risk factors and morbidities. Appropriate investigations like hemoglobin, blood counts, serum electrolytes, blood glucose, serum bilirubin (total and direct), full septic workup, CSF study, urine examination, stool for an occult blood test, chest X-ray, and Echocardiography were done to confirm the diagnosis. Data obtained were tabulated and necessary statistical analysis was done using SPSS 22 software. Descriptive statistics of the study population were generated by calculating percentages, mean and standard deviation.

RESULTS

A total of 162 patients were enrolled and analyzed in this study. The study was done into two groups; 1st is Appropriate for Gestational Age (AGA) and 2nd is Small for Gestational Age (SGA). Table-1 shows the characteristics features of the study population. The male was 8(54.32%) and the female was 74(45.68%). According to the birth weight proportion 106(65.43%) babies were from 1251-1499 gm weight range was the height, 41(12.31%) babies were from 1000-1250 gm weight range, 13(8.02%) babies were from 750-<1000 gm weight range and only two babies were from the range of <750 gm. The gestational age of the study is described in table-1; 83(51.23%) babies were from the range of 28-32 weeks, 54(33.33%) babies were from the age range >31-36, 13(8.02%) babies were from the range <28 and 12(7.41%) babies were from the range >36. From the birth weight according to gestational age 122(75.31%) babies were from AGA and 40(24.69%) babies were from SGA (Table-1). The plurality of the study was 117(72.22%) single babies, 17(10.49%) twin babies and 2(1.23%) triplet babies (Table-1). Table-2 shows the association of maternal risk factors with AGA and SGA babies; 122 babies wear from the AGA group and 40 babies were from the SGA group. The relative risk of complications in AGA and SGA babies of the study is represented in table-3 where 122 babies were from the AGA group and 40 babies were from the SGA group. Table-4 shows the relational outcome with antenatal steroids in the study. The antenatal steroid proportion is divided into given (N=69) and not given (N=93), the p-value of the incidence is 0.51 for RDS, 0.17 for NEC and 0.54 for IVH which are not significant. The last table of the result is describing the relative risk of complications in AGA and SGA babies; from the outcomes, 127 babies survived and 35 babies expired and the p-value was 0.059 which was a significant change (Table-5).

Table-1: Characteristic features of the study Group (N=162)

Characteristics	Frequency	Percentage
Gender		
Male	88	54.32
Female	74	45.68
Birth weight (gm)		
<750	2	1.23
750-<1000	13	8.02
1000-1250	41	25.31
1251-1499	106	65.43
Gestational age (weeks)		
<28	13	8.02
28-32	83	51.23
>32-36	54	33.33
>36	12	7.41
Birth Weight according to GA		
AGA	122	75.31
SGA	40	24.69
Number of pregnancy		
Single	117	72.22
Twin	17	10.49
Triplet	2	1.23
Place of birth		
In-born	155	95.68
Out-born	7	4.32

Table-2: Association of Maternal Risk Factors with AGA and SGA babies

Variables	AGA (N=122)		SGA (N=40)	
	N	%	N	%
Poor socio-economic condition				
Present	41	33.61	13	32.50
Absent	82	67.21	27	67.50
Maternal nutrition				
BMI <18.5 kg/m ²	8	6.56	4	10.00
BMI >18.5 kg/m ²	14	11.48	36	90.00
Short stature				
< 145 cm	12	9.84	5	12.50
>145 cm	110	90.16	35	87.50
Maternal Anemia				
Hb <11 g/dl	10	8.20	6	15.00
Hb >11 g/dl	12	9.84	34	85.00
Bad obstetric history				
Present	13	10.66	9	22.50
Absent	109	89.34	31	77.50
Maternal Hypertension				
Present	19	15.57	13	32.50
Absent	103	84.43	27	67.50
Chronic illness				
Present	10	8.20	5	12.50
Absent	112	91.80	35	87.50
Antenatal care				
>3 visit	70	57.38	24	60.00
<3 visit	52	42.62	16	40.00
Premature rupture of membrane				
Present	24	19.67	11	27.50
Absent	98	80.33	29	72.50
Cervical incompetence				
Present	2	1.64	1	2.50
Absent	120	98.36	39	97.50
Antepartum Hge				
Present	10	8.20	4	10.00
Absent	112	91.80	36	90.00

Table-3: Relative risk of complications in AGA and SGA babies

Variables	AGA (N=122)		SGA (N=40)	
	N	%	N	%
Respiratory distress syndrome (RDS)				
Yes	37	30.33	8	20.00
No	85	69.67	32	80.00
Apnoea				
Yes	34	27.87	7	17.50
No	88	72.13	33	82.50
Hypoxic Ischemic Encephalopathy				
Yes	9	7.38	3	7.50
No	113	92.62	37	92.50
Pul. Hemorrhage				
Yes	4	3.28	1	2.50
No	118	96.72	39	97.50
Polycythemia				
Yes	19	15.57	5	12.50
No	103	84.43	35	87.50
Jaundice				
Yes	36	29.51	12	30.00
No	86	70.49	28	70.00
Anemia				
Yes	10	8.20	4	10.00
No	112	91.80	36	90.00
(DIC)				
Yes	12	9.84	7	17.50
No	110	90.16	33	82.50
Sepsis				
Yes	29	23.77	7	17.50
No	93	76.23	33	82.50
Pneumonia				
Yes	8	6.56	3	7.50
No	114	93.44	37	92.50
Meningitis				
Yes	2	1.64	1	2.50
No	120	98.36	39	97.50
Hypoglycemia				
Yes	8	6.56	7	17.50
No	114	93.44	33	82.50
Hyperglycemia				
Yes	11	9.02	4	10.00
No	111	90.98	36	90.00
Acute Kidney Injury (AKI)				
Yes	1	0.82	0	0.00
No	121	99.18	40	100.00
Necrotizing enter colitis (NEC)				
Yes	8	6.56	2	5.00
No	114	93.44	38	95.00
Patent ductus arteriosus (PDA)				
Yes	22	18.03	6	15.00
No	100	81.97	34	85.00
Intraventricular hemorrhage (IVH)				
Yes	3	2.46	2	5.00
No	119	97.54	38	95.00

Table-4: Relation of outcome with antenatal steroids

Incidence		Antenatal steroid				Total	P-value
		Given (N=69)		Not given (N=93)			
		N	%	N	%		
RDS	Yes	18	26.09	27	29.03	45	0.52
	No	51	73.91	66	70.97	117	
NEC	Yes	5	7.25	4	4.30	9	0.17
	No	64	92.75	89	95.70	153	
IVH	Yes	2	2.90	3	3.23	5	0.54
	No	67	97.10	90	96.77	157	

Table-5: Relative risk of complication in AGA and SGA babies

Antenatal steroid	Outcome				Total	P-value
	Survived (N=127)		Expired (N=35)			
	N	%	N	%		
Given	58	45.67	12	34.29	70	0.059
Not given	69	54.33	23	65.71	92	
Total	127	100.00	35	100.00	162	

DISCUSSION

Due to the advance in prenatal and neonatal care now a day's more preterm and very low birth weight babies are surviving. However, published data on outcomes of very low birth weight infants from Bangladesh are limited. Morbidities and mortality of VLBW babies vary between countries and in different hospitals as a result of specific treatment patterns employed in individual intensive care units. Incidence of VLBW neonates (1.7%) in this report was lesser than in other countries; the worldwide prevalence of VLBW babies has been reported between 5-7% and that of ELBW as 1%; however, studies from the United States reported as 1.1% and 0.7% respectively [16]. This study was conducted in a level three NICU in a tertiary hospital; therefore, our figures may not represent the nationwide prevalence of very low birth weight infants. The majority (54.6%) of VLBW babies admitted were male which was much higher than the normal sex distribution of the general population of the country, probably indicating the preference of the parents to seek health care for the male babies. Mannan *et al.*, in Bangladesh, showed that 62.86% of VLBW babies in their study were male, values being quite similar to this study, showing male sex as a risk factor for VLBW delivery [17]. Maternal risk factors associated with the incidence of VLBW babies in this study were primiparity, PROM, hypertension, and under-nutrition. Undernutrition, hypertension, PROM, and APH were found to be associated more with the incidence of SGA babies in comparison to AGA babies Mannan *et al.*, Manganaro *et al.*, and Roy *et al.*, found similar risk factors as common associations contributing to the increased incidence of VLBW babies in varying percentages [4, 17-19]. The majority (76.4%) of VLBW babies in this study were preterm with a significant proportion (39.62%) being both preterm and SGA, the results being quite similar to previous studies suggesting that multiple factors were acting together

[16, 18]. Neonatal Jaundice, RDS, sepsis, apnoea, HIE, pulmonary hemorrhage, PDA, and NEC were found to be significant morbidities. Compared to the study of Mannan *et al.*, the incidence of jaundice and RDS were much higher in this study than in the incidence [17]. The incidence of IVH was quite similar in both studies. Ahmed *et al.*, showed the incidence of Jaundice needing phototherapy to be 26.7% whereas in this study the incidence was much higher (43.31%) [20]. Incidence of birth asphyxia was found to be much lower (20.43%) compared to their study reflecting improved perinatal care. Anemia was detected in 31 cases (9.68%) out of which 10 (5.38%) needed a blood transfusion in the present study, the incidence being comparable with the study of Ahmed *et al.*, Neubauer *et al.*, showed that 72% of mothers had been given antenatal corticosteroids for neonatal RDS prophylaxis, 46% of ELBW developed RDS and 41% received surfactant treatment. Raju *et al.*, showed the incidence of RDS as 12% at 33-34 weeks, 2% at 35-36 weeks and 0.11% at term in their study of the outcome of late preterm infants [21, 22]. The overall incidence of RDS was found to be much higher (28.08%) in this study probably due to poor coverage of antenatal steroids. However, exposure to antenatal steroids was found to be associated with improved survival and a significant reduction in the incidence of RDS, NEC, and IVH. Higher birth weight & gestational age and female sex were each found to be associated with improved survival which has been well established in previous studies [20]. Intraventricular hemorrhage (IVH) complicates subarachnoid hemorrhage (SAH) and intracerebral hemorrhage (ICH) in 15% and 40% of patients, respectively [21]. Several studies have identified ventricular dilation, intraventricular hematoma volume, and increased ICP to be indicators of poor prognosis in patients with IVH [26]. The rate of overall survival for VLBW newborns has been widely different in studies from different parts of the world, 63% from India, 35.6% from a study in Iran, 70% and

71%, and from South Africa, 74.5% from Turkey [27-29]. These differences are mainly related to gestational age, birth weight and associated diseases of the newborns, and standard care of NICU in different studies. Neonates weighing ≤ 700 gm at birth had the highest mortality rate. None of them survived, similar to other studies [29, 30]. Main cause of mortality in our patients was RDS leading to respiratory failure; perinatal asphyxia and sepsis were also common causes of death, which need improving quality of care in the antenatal, perinatal and postnatal periods of the newborn.

Limitations of the study

This was a hospital-based study and does not give a complete idea of the community at large. Further, follow-up studies are necessary to have a better understanding of the long-term outcome among the survivors.

CONCLUSION AND RECOMMENDATIONS

Proper antenatal and perinatal care is necessary to prevent the incidence of VLBW babies and the associated complications. Higher birth weight and gestational age, female sex, and exposure to antenatal steroids were associated with improved survival and reduction of morbidities. Widespread coverage with antenatal steroids should be done when preterm delivery is inevitable. Regular follow-up of the survivors for growth monitoring, neurodevelopmental assessment, and early detection of complications with prompt intervention, to have a neurologically intact outcome with a minimum disability will be highly appreciated and remain crucial.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee.

REFERENCES

1. Fanaroff, A. A., Stoll, B. J., Wright, L. L., Carlo, W. A., Ehrenkranz, R. A., Stark, A. R., ... & NICHD Neonatal Research Network. (2007). Trends in neonatal morbidity and mortality for very low birthweight infants. *American journal of obstetrics and gynecology*, 196(2), 147-e1.
2. United Nations. Department of Economic. The Millennium Development Goals Report 2008. United Nations Publications. Available at <http://www.un.org/en/development/desa/publications/millennium-development-goals-report-2008.html>
3. Negi, K. S., Kandpal, S. D., & Kukreti, M. (2006). Epidemiological factors affecting low birth weight. *JK science*, 8(1), 31-34.
4. Mangano, R., Gemelli, M., Mami, C., Mancuso, A., Rizza, M. L., & Leonardi, R. (1991). Analysis of factors associated with very low birth weight (less than or equal to 1500 g). *Minerva Ginecologica*, 43(6), 283-286.
5. National Neonatology Forum of India. (2002). National Neonatal Perinatal Database. Report 2002-03. New Delhi: National Neonatology Forum of India; 2002-03. p. 1-70.
6. March of Dimes, PMNCH, Save the Children, WHO. (2012). Born Too Soon: The Global Action Report on Preterm Birth. Eds CP Howson, MV Kinney, JE Lawn. World Health Organization. Geneva.
7. Naskar, N., Swain, A., Das, K. N., & Patnayak, A. B. (2014). Maternal risk factors, complications and outcome of very low birth weight babies: prospective cohort study from a tertiary care centre in Odisha. *J Neonatal Biol*, 3(10.4172), 2167-0897.
8. Eichenwald, E. C., & Stark, A. R. (2008). Management and outcomes of very low birth weight. *New England Journal of Medicine*, 358(16), 1700-1711.
9. DiPietro, J. A., & Allen, M. C. (1991). Estimation of gestational age: Implications for developmental research. *Child development*, 62(5), 1184-1199.
10. Lynch, C. D., & Zhang, J. (2007). The research implications of the selection of a gestational age estimation method. *Paediatric and perinatal epidemiology*, 21, 86-96.
11. Delpachitra, P., Palmer, K., Onwude, J., Meagher, S., Rombauts, L., Waalwyk, K., ... & Tong, S. (2012). Ultrasound reference chart based on IVF dates to estimate gestational age at 6-9 weeks' gestation. *International Scholarly Research Notices*, 2012, 938583.
12. Sasidharan, K., Dutta, S., & Narang, A. (2009). Validity of New Ballard Score until 7th day of postnatal life in moderately preterm neonates. *Archives of Disease in Childhood-Fetal and Neonatal Edition*, 94(1), F39-F44.
13. Fenton, T. R. (2003). A new growth chart for preterm babies: Babson and Benda's chart updated with recent data and a new format. *BMC pediatrics*, 3(1), 1-10.
14. Volpe, J. J. (1989). Intraventricular hemorrhage and brain injury in the premature infant: neuropathology and pathogenesis. *Clinics in perinatology*, 16(2), 361-386.
15. Walsh, M. C., & Kliegman, R. M. (1986). Necrotizing enterocolitis: treatment based on staging criteria. *Pediatric Clinics of North America*, 33(1), 179-201.
16. Butler, A. S., & Behrman, R. E., editors. (2007). Preterm birth: causes, consequences, and prevention. National Academies Press.
17. Mannan, M. A., Jahan, N., Dey, S. K., Uddin, M. F., & Ahmed, S. (2012). Maternal and foetal risk factor and complication with immediate outcome during hospital stay of very low birth weight babies. *Mymensingh medical journal: MMJ*, 21(4),

- 639-647.
18. Manganaro, R., Gemelli, M., Mami, C., Mancuso, A., Rizza, M. L., & Leonardi, R. (1991). Analysis of factors associated with very low birth weight (less than or equal to 1500 g). *Minerva Ginecologica*, 43(6), 283-286.
 19. Roy, K. K., Baruah, J., Kumar, S., Malhotra, N., Deorari, A. K., & Sharma, J. B. (2006). Maternal antenatal profile and immediate neonatal outcome in VLBW and ELBW babies. *The Indian Journal of Pediatrics*, 73(8), 669-673.
 20. Ahmed, A. N. U., Rob, M. A., Rahman, F., Rahman, R., & Huda, N. (2008). Preterm Very Low-Birth Weight Babies: Outcome of Admitted Newborns at a Community-Level Medical College Hospital in Bangladesh. *Journal of Bangladesh College of Physicians and Surgeons*, 26(3), 128-134.
 21. Zhu, X. L., Chan, M. S. Y., & Poon, W. S. (1997). Spontaneous intracranial hemorrhage: which patients need diagnostic cerebral angiography? A prospective study of 206 cases and review of the literature. *Stroke*, 28(7), 1406-1409.
 22. Raju, T. N., Higgins, R. D., Stark, A. R., & Leveno, K. J. (2006). Optimizing care and outcome for late-preterm (near-term) infants: a summary of the workshop sponsored by the National Institute of Child Health and Human Development. *Pediatrics*, 118(3), 1207-1214.
 23. Committee on Fetus and Newborn. (2002). Postnatal corticosteroids to treat or prevent chronic lung disease in preterm infants. *Pediatrics*, 109(2), 330-338.
 24. Lemons, J. A., Bauer, C. R., Oh, W., Korones, S. B., Papile, L. A., Stoll, B. J., ... & NICHD Neonatal Research Network. (2001). Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. *Pediatrics*, 107(1), e1-e1.
 25. Zhang, H., Fang, J., Su, H., & Chen, M. (2011). Risk factors for bronchopulmonary dysplasia in neonates born at ≤ 1500 g (1999–2009). *Pediatrics International*, 53(6), 915-920.
 26. Mayfrank, L., Lippitz, B., Groth, M., Bertalanffy, H., & Gilsbach, J. M. (1993). Effect of recombinant tissue plasminogen activator on clot lysis and ventricular dilatation in the treatment of severe intraventricular haemorrhage. *Acta neurochirurgica*, 122(1), 32-38.
 27. Basu, S., Rathore, P., & Bhatia, B. D. (2008). Predictors of mortality in very low birth weight neonates in India. *Singapore medical journal*, 49(7), 556.
 28. Navaei, F., Aliabady, B., Moghtaderi, J., Moghtaderi, M., & Kelishadi, R. (2010). Early outcome of preterm infants with birth weight of 1500 g or less and gestational age of 30 weeks or less in Isfahan city, Iran. *World Journal of Pediatrics*, 6(3), 228-232.
 29. Canbak, Y., Silfeler, I., Dorum, B. A., Kurnaz, H., & Dorum, S. (2011). The ratio of mortality and morbidity in very low birth weight infants in a public hospital/Bir devlet hastanesinde cok dusuk dogum agirlikli yenidoğanlarda hastalik ve olum oranlari.(Original Article/Ozgun Arastirma). *Turkish Pediatrics Archive*, 144-151.
 30. Battin, M. R., Knight, D. B., Kuschel, C. A., & Howie, R. N. (2012). Improvement in mortality of very low birthweight infants and the changing pattern of neonatal mortality: The 50-year experience of one perinatal centre. *Journal of paediatrics and child health*, 48(7), 596-599.