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Incidence and predictors of respiratory distress syndrome among low birth weight neonates in the first seven days in Northwest Ethiopia Comprehensive Specialized Hospitals, 2023: A retrospective follow-up study

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ABSTRACT

Introduction Respiratory distress syndrome is a catastrophic respiratory problem among low birth weight neonates. It increases the suffering of neonates and the economic expenditure of the countries. Notably, it is a major public health issue in low-income and middle-income countries such as Ethiopia. Despite this, studies regarding respiratory distress syndrome among low birth weight neonates were limited in Ethiopia.

Objective To assess the incidence and predictors of respiratory distress syndrome among low birth weight neonates in the first 7 days in Northwest Ethiopia Comprehensive Specialized Hospitals.

Method Multicentred institution-based retrospective follow-up study was conducted from 19 September 2021 to 1 January 2023, among 423 low birthweight neonates. A simple random sampling technique was used. The data were collected using a data extraction checklist from the medical registry of neonates. The collected data were entered into EPI-DATA V.4.6.0.6. and analysed using STATA V.14. The Kaplan-Meier failure curve and log-rank test were employed. Bivariable and multivariable Weibull regression was carried out to identify predictors of respiratory distress syndrome. Statistical significance was declared at a $p\leq0.05$.

Result The incidence rate of respiratory distress syndrome was found to be 10.78 (95% CI 9.35 to 12.42) per 100 neonate days. Fifth minute Appearance, Pulse, Grimace, Activity, Respiration (APGAR score) <7 (AHR 1.86; 95% CI 1.18 to 2.92), multiple pregnancy (AHR 1.43; 95% CI 1.04 to 1.96), caesarean section delivery (AHR 0.62; 95% CI 0.41 to 0.93), prematurity (AHR 1.56; 95% CI 1.06 to 2.30) and birth weight <1000 g (AHR 3.14; 95% CI 1.81 to 5.40) and 1000–1499 g (AHR 2.06; 95% CI 1.42 to 2.83) were significant predictors.

Conclusion The incidence of respiratory distress syndrome was higher than other studies conducted on other groups of neonates. Multiple pregnancy, fifth minute APGAR score, caesarean section, prematurity, extremely low birth weight and very low birth weight were predictors of respiratory distress syndrome. However, it needs further prospective study. Therefore, the concerned stakeholders should give due attention and appropriate intervention for these predictors.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study was conducted in multicentres (five hospitals), and it covers a diverse population, which increases generalisability and shows the relationship between exposure and outcome variables.
- ⇒ Due to its retrospective nature, important variables, such as maternal nutritional status, family income and educational level, were missed.
- ⇒ In addition, the hospital's service context and supplies were not assessed.

BACKGROUND

Respiratory distress syndrome (RDS) is one of the major catastrophic and challenging respiratory problems among Low Birth Weight (LBW) neonates.[1 2] RDS has a devastating course with different morbidity, and it escalates to mortality.[3 4] Among LBW neonates, this problem causes significant admission in Neonatal Intensive Care Unit (NICU) ranging from 24.9% to 62.96%,[2 3 5–7] and 31.3% of death in the perinatal period.[8] According to the American Academy of Pediatrics, 15% of term, and 29% of preterm neonates admitted to NICU develop RDS.[9] The burden of this respiratory problem is high in low-income and middle-income countries, notably, in Southeast Asia and sub-Saharan African countries, including Ethiopia.[10] In East Africa, RDS is a common morbidity and it increases the probability of mortality three times in LBW neonates.[4]

The magnitude of RDS among LBW neonates varies across countries depending on the availability of medical services and the number of trained medical personnel. For instance, in Taiwan 60%–86%,[11 12] Finland 76%,[13] Thailand 70.7%,[14] Karachi, Pakistan 11%–12.8%,[15 16] Iran 76%,[17] Afghanistan 58.8%[18] and in Nigeria 10.9%[19] of LBW neonates had RDS. In Ethiopia, RDS is the primary cause of admission with a mortality rate of 45.3% among LBW neonates.[20] These studies showed that different factors increase the risk of RDS among LBW neonates. Accordingly, maternal Diabetes Mellitus (DM),[21–23] hypertension,[21] mode of delivery,[18 21 22 24] sex,[12 18 21 22 24] prematurity,[12 18 21 22] multiparity[24] birth weight,[12 18 22] antenatal steroid,[12 25] hyperglycaemia,[26] sepsis,[18] Antepartum Paemorrhage (APH),[18] Premature Rupture of Membrane (PROM),[18 27] first and fifth minute ((Appearance, Pulse, Grimace, Activity, Respiration) (APGAR)) score[28] were significant predictors of RDS.

To alleviate this problem and reduce newborn morbidity and mortality, World Health Organization(WHO) recommends the use of antenatal corticosteroid therapy for risky women, Kangaroo mother care, Continuous Positive Airway Pressure (CPAP), tocolytics for preterm labour and optimal oxygen therapy,[29] Furthermore, the Federal Ministry of Health has given due attention in the expansion of high-quality neonatal care to reduce neonatal morbidity like RDS.[30] Despite these efforts, RDS continues to be a major public health problem by increasing neonate suffering, and mortality, and escalating economic expenditures in low-income and middle-income countries, including Ethiopia.

Some studies were conducted regarding RDS inclusive of all neonates, However, studies regarding RDS, notably among LBW neonates, were limited in Ethiopia. Hence, this retrospective study aimed to assess the incidence and predictors of RDS among LBW in the first seven days of life in Northwest Ethiopia Comprehensive Specialised Hospitals. The findings of this study will provide new insight for different stakeholders, and it will help health professionals understand the significant predictors of RDS. Additionally, it will serve as baseline information for future studies, and it will give clues to mobilise resources towards the predictors of RDS.

METHODS

Stud design and period

An institution-based multicentred retrospective follow-up study was carried out from 19 September, 2021 to 1 January 2023 (the data were retrospectively extracted from 5 January 2023 to 19 February 2023).

Study setting

The study was conducted in the NICU of Northwest Ethiopia Comprehensive Specialized Hospitals. These hospitals are the University of Gondar Comprehensive Specialized Hospital (UoGCSH), Felege hiwot, Tibebe Ghion, Debre Tabor and Debre Markos Comprehensive Specialized Hospital. UoGCSH is found in Gondar town, this hospital has an average annual admission of 697 LBW neonates in their first week of life. Felege hiwot and Tibebe Ghion CSH are found in Bahir Dar city, These, hospitals have an average annual admission of 675, and 683 LBW neonates in their first week of life respectively. Debre Tabor CSH is found in Debre Tabor town, with an average annual admission of 560 LBW neonates in their first 7 days of life. Debre Markos CSH is found in Debre Markos town, with an average annual admission of 594 LBW early neonates. These hospitals have NICUs with different health professionals (paediatricians, neonatologists, general practitioners, comprehensive nurses, paediatrics and neonatal nurses). This team in collaboration provides a diagnosis of the neonate's problem and holistic care including documentation. The major services in the NICU of these hospitals include general neonatal care services, blood and exchange transfusion, phototherapy, ventilation support such as Continuous Positive Air Pressure (CPAP, and other routine neonatal care.

Study population

All LBW neonates in the first 7 days of life admitted to the NICU of Northwest Ethiopia comprehensive specialized hospitals were the source population.

All LBW neonates in the first 7 days of life admitted to the NICU of Northwest Ethiopia Comprehensive Specialized Hospitals from 19 September 2021 to 1 January 2023, were taken as a study population.

Inclusion and exclusion criteria

LBW neonates in the first week of life who were admitted to NICU from 19 September 2021 to 1 January 2023, were included, whereas, neonates with an incomplete chart (outcome status and charts with one missed predictor of the following (gestational age, birth weight, neonatal age, sex, type of pregnancy, date of admission and discharge)), and neonates with major respiratory and cardiovascular malformation were excluded.

Sample size determination and sampling procedure

The minimum required sample size was determined using the single population proportion formula by considering the following statistical assumptions za/2=the corresponding Z score of 95% CI, and d=margin of error (5%), and proportion of RDS(P) (50%). The proportion of RDS was taken as 50% because there were no previous studies regarding the incidence of RDS among LBW neonates in the study setting. Therefore,

$$n = \frac{(\frac{Za}{2})^2\ p(1-p)}{d^2}$$

$$n = \frac{(1.96)^2\ (0.5)(0.5)}{(0.05^2)}$$

So, $n = 384.16$.

Then, the incompleteness of medical records (chart attrition) was taken as 10%. Accordingly, the final estimated sample size was 422.576=423. So, a total of 423 medical records of LBW neonates were reviewed. The total sample size was proportionally allocated to each hospital. Then the neonate's chart was selected by a simple random sampling technique using computer-generated random number.

Variables of the study

Dependent variable: RDS in the first 7 days of life. It was dichotomised into RDS (event of interest=1) and censored (no RDS=0).

Independent variables: (1) Sociodemographic, medical and obstetric characteristics of mothers of LBW neonates such as maternal age, place of delivery, residence, type of pregnancy, gravidity, PROM, APH, mode of delivery, pre-eclampsia, Antenatal Care (ANC) follow-up, corticosteroid administration, DM, chronic hypertension, HIV/AIDS, anaemia and (2) neonate's clinical and other characteristics such as sex of the neonate, age of the neonate, perinatal asphyxia (PNA), sepsis, jaundice, hypothermia, hypoglycaemia, Necrotising Enter Colitis (NEC), first and fifth minute APGAR score, breast feeding, congenital anomalies, IntraUterine Growth Restriction (IUGR), birth weight and gestational age.

Operational definition

LBW: Weight at birth less than 2500 g regardless of gestational age.[31]

RDS: It is defined as the presence of the following two or more signs: abnormal respiratory rate, expiratory grunting, nasal flaring and chest wall recession with or without cyanosis.[32]

Event: LBW neonates who develop RDS during the follow-up.

Censored: LBW neonates who did not develop RDS, discharged against medical advice, died, transferred/referred and lost the follow-up during the follow-up.

Extremely LBW: Neonates born with less than 1000 g of birth weight.[31]

Follow-up time: The time from admission to NICU to either death or censorship occurs.

Prematurity: Neonate born before 37 completed weeks of gestational age.[33]

Very LBW: Neonates born with (1000–1499 g) of birth weight.[33]

Data abstraction checklist and procedures

The data were collected using a data abstraction checklist which was adapted by reviewing different literature[2 33–36] (online supplemental file 1). The neonates were followed from the time of admission until either the event of interest was developed or censored. The data were collected retrospectively by five BSc nurses and supervised by five experienced BSc nurses. The required number of neonates' medical charts was selected by a simple random sampling technique.

Data quality control

To ensure the quality of the data, the data abstraction checklist was evaluated by a research expert, and a pretest was done on 5% of the sample size. Based on the pretest findings necessary modifications were done. One-day training was given to data collectors and supervisors about the purpose of the study, the data collection tool, data collection methods and ethical concerns during data collection. All the collected data were checked for completeness and consistency by the data collector and supervisors.

Data processing and analysis

Data were entered into Epi-Data V.4.6.0.6 and exported to STATA V.14 statistical software for cleaning, coding and analysis. Descriptive measures such as mean with SD, median with IQR, percentage and frequency were used to characterise the data.

The incidence rate of RDS was calculated for the entire follow-up by dividing the total number of new cases of LBW neonates with RDS by the total neonates-day of follow-up (time at risk). Kaplan-Meier failure curve was used to estimate the time to develop RDS. The log-rank test was employed to compare statistical differences between independent variables. The Proportional Hazard Assumption (PHA) was checked using both graphical and hypothesis tests (Schoenfeld residual test) for all predictors, and it revealed that the PHA was satisfied. The log-likelihood and Akaike Information Criteria (AIC) were applied to select the best-fitted model, and a model with minimum AIC was considered the best-fitted model. Based on this, the Weibull regression model with the (AIC=713.5962) value was the best-fitted model. In addition, the goodness-of-model fitness was also checked using the Cox-Snell residual test, and it was close to the 45° line. Variables having a $p<0.25$ in the bivariable analysis were fitted into the multivariable Weibull regression model. Hazard Ratio (HR) with 95% CI were used to determine the strength of the association. Variables having a $p<0.05$ in multivariable analysis were considered statistically significant.

Patient and public involvement

In this study, the study participants and/or public were not directly involved in the design, conduct, reporting and dissemination of this work.

RESULTS

Sociodemographic, medical and obstetric characteristics of mothers of LBW neonates

A total of 423 LBW neonates' charts were reviewed, and 405 (95.74%) met the enrolment criteria. In this study, two-thirds of the mothers 274 (67.65%) were in the age group of 21–34 years old with a mean of 27.4(SD±6) years old, and 226 (55.80%) were from urban areas. Among the total enrolled mothers, 301 (74.32%) had given birth through spontaneous vaginal delivery, and three-fourths 304 (75.06%) of pregnancies were singleton. In this study, the majority of mothers 375 (92.59%) had ANC follow-ups in nearby health institutions, and one-fourth 302 (75.557%) of them had pre-eclampsia. Moreover, 82 (20.25%) mothers had taking corticosteroid treatment, and 16 (4.69%) had HIV/AIDS infection (table 1).

Clinical and other characteristics of LBW neonates

In this study, over half of the participants 218 (53.83%) were male, and 279 (68.89%) were admitted within 24 hours of

Table 1 Sociodemographic, medical and obstetric characteristics of mothers of low birthweight neonates admitted at NICU of Northwest Ethiopia CSH from (19 September 2021 to 1 January 2023) (N=405)

Variables		Frequency	Per cent
Maternal age	≤20 years	66	16.30
	21–34	274	67.65
	≥35	65	16.05
Residence	Urban	226	55.80
	Rural	179	44.20
Place of delivery	Health institution	389	55.80
	Out-of-health institution	16	44.20
ANC follow-up	Yes	375	92.59
	No	30	7.14
Types of pregnancy	Single	304	75.06
	Multiple	101	24.94
Mode of delivery	SVD	301	74.32
	Instrumental	16	3.95
	Caesarean section	88	21.73
Gravidity	Prim gravida	78	19.26
	Multi gravida	327	80.74
Pre-eclampsia	Yes	302	75.57
	No	103	24.43
Corticosteroid treatment	Yes	82	20.25
	No	323	79.75
PROM	Yes	55	13.58
	No	350	86.42
APH	Yes	41	10.12
	No	364	89.88
Chronic hypertension	Yes	12	2.96
	No	393	97.04
Maternal DM	Yes	3	0.74
	No	402	99.26
Maternal HIV infection	Reactive	19	4.69
	Non-reactive	386	95.31
Maternal anaemia	Anaemic	5	1.23
	Non-anaemic	400	98.77

ANC, antenatal care; APH, antepartum haemorrhage; CSH, Comprehensive Specialised Hospital; DM, diabetes mellitus; NICU, neonatal intensive care unit; PROM, premature rupture of membrane; SVD, spontaneous vaginal delivery.

birth. Regarding birth weight, three-fourths of neonates were between 1500 and 2499 g with a median weight of 1715 (IQR 800–2478). Above two-thirds 279 (68.89%) of neonates were premature, and the mean gestational age was 34.7 weeks with (SD±3.3). The common medical problems among LBW early neonates were sepsis 283 (69.88%) and hypothermia 155 (38.27%). The other medical problems include jaundice, PNA, NEC, IUGR, hypoglycaemia and other congenital anomalies (table 2).

Proportional Hazard Assumption (PHA) test

The PHA was checked using the Schoenfeld residuals test. The test showed that the p value for each covariate and the whole covariates simultaneously were above 0.05 (p=0.6298).

Incidence of RDS and overall outcome of the follow-up

In this study, the neonates were followed for up to 7 completed days of age starting from the date of admission. The total number of neonate days' observations during the entire follow-up was 1771 neonate day observations. The total neonate's day observation (1771) was the sum of each neonate's time at risk during the follow-up (ie, the sum of the length of time in day each neonate was followed during the study). From the total enrolled LBW early neonates, during the follow-up 47.16% (95% CI 42.80% to 52.55%) developed the event of interest (RDS). The proportion of RDS was 38.37% for the UoGCSH, 50.00% for Feleghiwot Comprehensive Specialized Hospital, 43.24% for Tibebe Ghion Hospital, 58.14% for Debre Markos Hospital and 45.07% for Debre Tabor Comprehensive Specialized Hospital.

In this study, the overall incidence rate of RDS was found to be 10.78 per 100 neonates' day observation (95% CI 9.35 to 12.42). The incidence of RDS at the end of 24 hours, 2nd, 3rd, 4th, 5th, 6th and 7th days were 52.63, 26.72, 16.66, 10.63, 9.5, 7.99 and 5.91 per 100 neonate's day observation, respectively. Similarly, the incidence of RDS among extremely low birth weight (ELBW) (<1000 g), very low birth weight (VLBW) (1000–1499 g) and LBW (1500–2499) was 25.39, 18. 98, and 8.26 per 100 neonate's day observation, respectively (table 3).

Overall failure function (survivorship function)

In this study, the median length of hospital stay was 6 days (95% CI 6 to 7), and the maximum follow-up time was 7 days. The overall Kaplan-Meier failure function showed that the probability of developing RDS was increasing as follow-up time increased. The cumulative probability of developing RDS at the end of the 1st day was 0.1630 (95% CI 0.1304 to 0.2027), at the end of the 3rd day was 0.3383 (95% CI 0.2945 to 0.3866) and at the end of the 7th day was 0.7704 (95% CI 0.7284 to 0.8100) (figure 1).

Comparison of failure function for some variables

In this study, neonates having ELBW (<1000 g) and VLBW (1000–1499 g) had a higher risk of developing RDS than LBW neonates (1500–2499 g). The mean hazard time for EVLBW and VLBW was 3.36 days and 4.11 days, respectively, as compared with those LBW neonates with a mean hazard time of 5.52 days. This study also revealed that premature neonates had a higher risk of developing RDS as compared with their counterparts. The mean hazard time to develop RDS was 4.84 days. Furthermore, neonates with fifth minute APGAR scores less than <7 had a higher probability of developing RDS as compared with

Table 2 Clinical and other characteristics of low birthweight early neonates admitted to Northwest Ethiopia CSH from 19 September 2021 to 1 January 2023) (N=405)

Variable		Frequency	Per cent
Sex	Male	218	53.83
	Female	187	46.17
Age of the neonate at admission in days	≤1	279	68.89
	2–3	76	18.77
	4–7	50	12.35
Gestational age in a week	< 37	279	68.89
	≥37	126	31.11
Birth weight	≤999	21	5.19
	1000–1499	84	20.74
	1500–2499	300	74.07
Breast feeding	Yes	384	94.81
	No	21	5.91
First minute APGAR score	<7	153	37.78
	≥7	252	62.22
Fifth minute APGAR score	<7	46	11.36
	≥7	359	88.64
Sepsis	Yes	283	69.88
	No	122	30.12
PNA	Yes	56	13.83
	No	349	86.17
NEC	Yes	17	4.20
	No	388	95.80
Jaundice	Yes	61	15.06
	No	344	84.94
Congenital anomaly	Yes	22	5.42
	No	383	94.57
Hypothermia	Yes	155	38.27
	No	250	61.73
IUGR	Yes	17	4.20
	No	388	95.80
Hypoglycaemia	Hypoglycaemic	14	3.46
	Non-hypoglycaemic	391	96.54

APGAR, Appearance, Pulse, Grimace, Activity, Respiration; CSH, Comprehensive Specialised Hospital; IUGR, intrauterine growth restriction; NEC, necrotising entero colitis; PNA, perinatal asphyxia.

their counterparts. These differences were statistically significant with a (p<0.0006) in the log-rank test (online supplemental figure 1).

Model comparison and diagnostics

To select the most parsimonious models for the data set, a comparison of the semiparametric and parametric hazard models was done statistically using Akakie and Bayesian Information Criterion (AIC,BIC) and graphically using the Cox-Snell residual test. Based on this, the Weibull regression model with (AIC=713.5962) was the parsimonious model than the parametric exponential (AIC=772.3843), Gompertz (AIC=721.98) and semiparametric Cox proportional hazard models (AIC=2064.185). So, all of the interpretations in this study were using the Weibull regression model.

The goodness of fit for the fitted model was also checked using the Cox-Snell residual test, and as shown in the figure, Weibull regression model was adequate (figure 2).

Predictors of RDS

In the bivariable Weibull regression, sex, mode of delivery, preeclampsia, PNA, NEC, IUGR, first and fifth-minute APGAR score, birth weight, gestational age and type of

Table 3 Incidence rate to birth weight and number of follow-up days among low birthweight neonates in Northwest Ethiopia CSH from 19 September 2021 to 1 January 2023) (N=405)

Variables	Category	RDS	Rate with (95% CI) per 100
Birth weight	ELBW	15	25.39 (15.55 to 41.45)
	VLBW	60	98 (14.74 to 24.45)
	LBW	118	8.26 (6.88 to 9.18)
No of follow-up days	1 day	30	52.63 (36.80 to 75.27)
	2 days	31	26.72 (18.79 to 38.00)
	3 days	23	16.66 (11.07 to 25.08)
	4 days	18	10.63 (6.60 to 17.09)
	5 days	19	9.5 (6.05 to 14.89)
	6 days	23	7.99 (53.07 to 12.01)
	7 days	48	5.91 (4.45 to 7.84)
Total incidence density			10.78 (9.35 to 12.42).

CSH, Comprehensive Specialised Hospital; ELBW, extremely low birth weight ; LBW, low birth weight; RDS, respiratory distress syndrome; VLBW, very low birth weight.

pregnancy were associated with RDS (p<0.25). However, in the multivariable Weibull regression analysis only five variables were significant predictors of RDS (p<0.05). Accordingly, the hazard of developing RDS was 1.43 times higher (Adjusted Hazard Ratio(AHR 1.43; 95% CI 1.04 to 1.96)) among neonates with multiple births as compared with singleton births. Similarly, neonates with APGAR scores <7 at the fifth minute were 1.86 times (AHR 1.86; 95% CI 1.18 to 2.92)) more likely to develop RDS as compared with neonates with normal APGAR scores.

Moreover, neonates delivered via caesarean section were 62% times (AHR 0.62; 95 CI 0.41 to 0.93) more likely to develop RDS as compared with their counterparts. Additionally, neonates with birth weights less than 1000 g and 1000–1499 g were three times (AHR 3.14; 95% CI 1.81 to 5.40) and two times (AHR 2.06; 95% CI 1.42 to 2.83)) at high risk of developing RDS as compared with their counterparts respectively. Finally, this study found that LBW early neonates who are preterm were 1.56 times (AHR 1.56; 95% CI 1.06 to 2.30) at a higher risk of developing RDS as compared with that of term neonates (table 4).

DISCUSSION

This study aimed to assess the incidence of RDS, and its predictor among LBW neonates admitted to Northwest Ethiopia Comprehensive Specialized Hospitals. Accordingly, this study found that at the end of the follow-up 47.16% (95% CI 42.80% to 52.55%) of neonates developed RDS. This finding was aligned with studies conducted in Thailand (44.15%),[37] and Ethiopia 49.8 3%,[38] The possible justification is due to similarities in study design, sample size and the presence of similar maternal health problems. On the other hand, this study was higher than two different studies conducted in Pakistan 11%–12.8%,[15 16] India 38%,[39] Nepal 21.4%[40] and Nigeria 10.9%.[19] The possible reason for this discrepancy is due to exclusion criteria. In those studies, neonates with any type of congenital disorders, and intrauterine

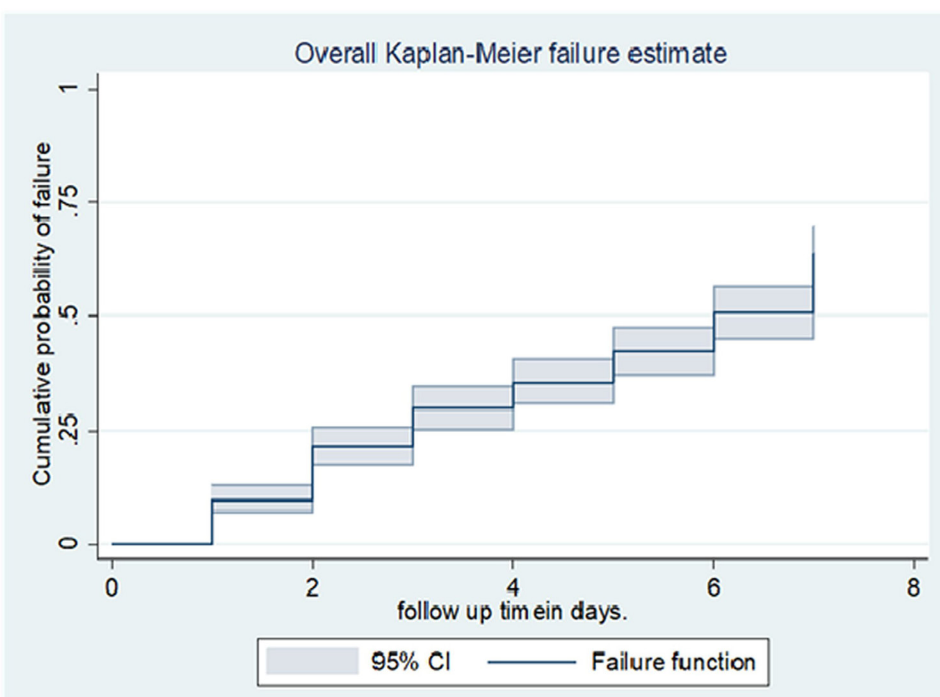

Figure 1 The overall Kaplan-Meier failure estimate curve with a 95% CI showing the time of developing Neonatal RDS in Northwest Ethiopia Comprehensive Specialized Hospital, 2023. RDS, respiratory distress syndrome.

Wondie WT, et al. BMJ Open 2023;13:e079063. doi:10.1136/bmjopen-2023-079063

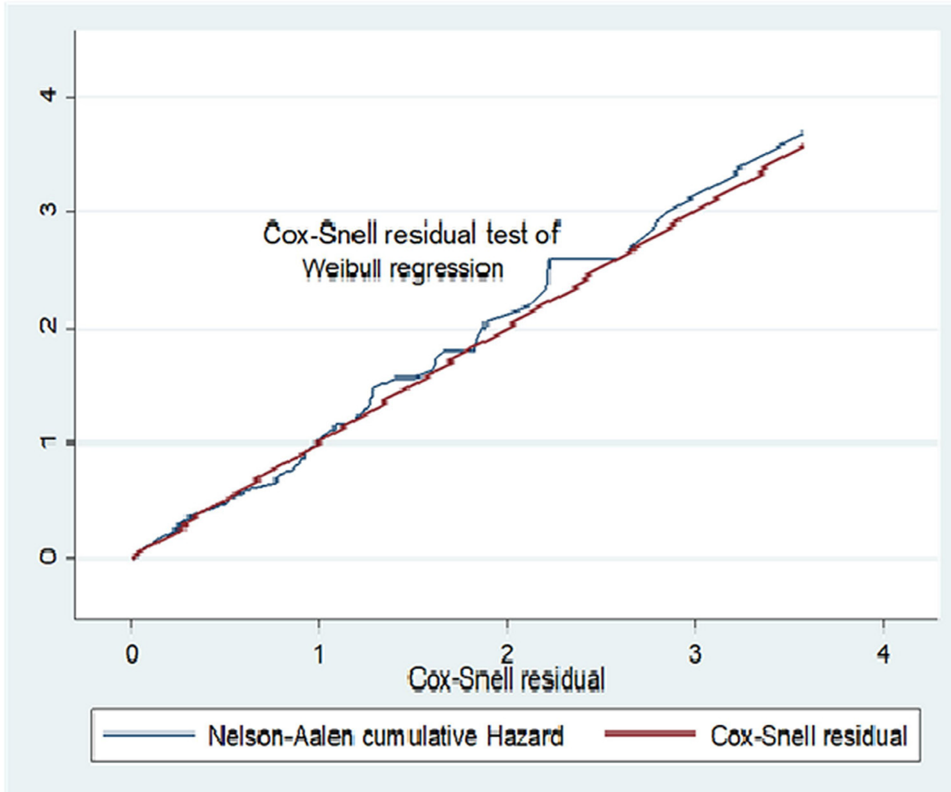

Figure 2 The Cox-Snell residual test of Weibull regression for Incidence of RDS. RDS, respiratory distress syndrome.

infection were excluded. But, the present study did not exclude those neonates. The second possible reason might be the diagnostic criteria, in those studies, they diagnose and include neonates who develop RDS within 4 hours of birth. Whereas, the present study considers neonates who develop RDS at any time of age during the follow-up. In addition to the above reasons, it might be due to the presence of skilled/trained medical teams in NICU across different departments to provide essential newborn care and postnatal care.[41] Furthermore, it might be due to their advanced NICU setups, like the availability of bubble CPAP, surfactant therapy and advanced treatment technologies.[42]

In contrast to the aforementioned studies, the present study was lower than studies conducted in Iran 76%,[17] Taiwan 60%–86.5%,[11 12] Thailand 70.7%,[14] Finland 76%[13] and Afghanistan 58.8%.[18] This marked difference might be attributed to study subject recruitment criteria, because those studies include only very LBW and very preterm neonates, so due to anatomical and physiological organ immaturity the probability of RDS could be high.[33 42] Whereas, the present study includes all categories of LBW and all categories of gestational age. The second possible explanation could be in those studies the magnitude of maternal morbidity such as DM, and pre-eclampsia/eclampsia was high.[23 42] In addition, in those studies, congenital anomalies were high in percentage, whereas in the present study, it was low.[18]

In this study, the incidence of RDS was found to be 10.78 per 100 neonate's day (95% CI 9.35 to 12.42) with 1771 neonate day observations. The incidence of RDS at the end of 24 hours, 2nd, 3rd, 4th 5th, 6th and 7th days were 52.63, 26.72, 16.66, 10.62, 9.5, 7.98, 5.91 per 100 neonate's day observation respectively. Similarly, the incidence of RDS among ELBW (<1000 g), VLBW (1000–1499 g) and LBW (1500–2499) was 25.39 (95% CI 15.55 to 41.45), 18.98 (95% CI 14.74 to 24.45) and 8.26 (95% CI 6.88 to 9.18) per 100 neonate's day observation respectively. Accordingly, the incidence of RDS was high, and the highest incidence rate of RDS was observed within 24 hours of birth, this is due to the difficulty of adapting to the extra uterine environment secondary to anatomical and physiological organ immaturity,[32] and lack of quality care immediately after birth.[32 42] Moreover, it might be due to antenatal, and intrapartum birth complications too.[1]

Being delivered through caesarean section is an independent predictor in this study and raises the risks of RDS in neonates with LBW. This finding is supported by Studies conducted in France,[43] China,[44 45] Taiwan,[12] Korea,[24] Qatar[46] and Egypt.[21] The possible justification is the residual amount of lung fluid in newborns who were delivered by caesarean section is greater, they produce less surfactant to the alveolar surface, and their lung fluid clearance is delayed.[47 48] The other justification is following a caesarean section, amiloride-sensitive sodium channels in alveolar epithelial cells are less active, which results in impaired fluid evacuation.[49]

In agreement with studies conducted in Taiwan,[12] Afghanistan,[18] Saudi Arabia[21] and China,[27] prematurity

Table 4 ; Bivariable and multivariable Weibull regression analysis for predictors of RDS among low birthweight neonates in their first 7 days of life in Northwest Ethiopia Comprehensive Specialised Hospitals from 19 September 2021 to 1 January 2023 (n=405)

Variable	Status: Event	Status: Censored	CHR (95%CI)	AHR (95%CI)
Sex				
Male	95	123	0.78 (0.59 to 1.03)	0.82 (0.61 to 1.10)
Female	98	89	1	1
Mode of delivery				
Instrumental assisted	6	10	0.50 (0.22 to 1.13)	0.48 (0.205 to 1.32)
CS	35	53	**0.60 (0.42 to 0.87)**	**0.62 (0.41 to 0.93)****
SVD	152	149		**1**
Type of pregnancy				
Multiple	60	41	**1.50 (1.10 to 2.04)**	**1.43 (1.04 to 1.96)****
Single	133	171		**1**
Pre-eclampsia				
Yes	52	51	1.17 (0.85 1.61)	1.14 (0.80 to 1.62)
No	141	161	1	1
PNA				
Yes	28	28	1.24 (0.83 to 1.85)	1.26 (0.82 to 1.94)
No	165	184	1	1
NEC				
Yes	10	7	1.44 (0.76 to 2.72)	1.40 (0.73 to 2.69)
No	183	205	1	1
IUGR				
Yes	5	13	0.39 (0.14 to 1.03)	0.67 (0.24 to 186)
No	188	199	1	1
First-minute APGAR score				
<7	85	68	1.48 (1.11 to 1.97)	1.08 (0.77 to 1.51)
≥7	108	144	1	1
Fifth-minute APGAR score				
<7	32	14	**1.94 (1.33 to 2.83**)	**1.86 (1.18 to 2.92)*****
≥7	161	198	**1**	1
Gestational age in weeks				
<37	156	123	**2.09 (1.43 to 3.05)**	**1.56 (1.06 to 2.30)****
≥37	37	89	1	1
Birth weight				
≤999	15	6	**3.52 (2.11 to 5.86)**	**3.14 (1.81 to 5.40)*****
1000–1499	60	24	**2.43 (1.78 to 3.33)**	**2.06 (1.42 to 2.83)****
1500–2499	118	182	**1**	1

**=Statistically significant variables with p-value <0.01, & ***p<0.001.
1, reference; AHR, Adjusted Hazard Ratio; APGAR, Appearance, Pulse, Grimace, Activity, Respiration; CHR, Crude Hazard Ratio; CS, caesarean section; IUGR, intrauterine growth restriction; NEC, necrotising entero colitis; PNA, perinatal asphyxia; SVD, spontaneous vaginal delivery.

is a predictor of RDS. This is explained by due to inadequate surfactant production or inactivation of surfactant in the context of immature lungs. Due to this, the synthesised surfactant is not adequate to maintain alveolar stability, and this leads to atelectasis, and the neonate develops RDS.[32 33 50] In addition, premature neonates are more vulnerable to different medical problems such as hypothermia, hypoglycaemia, sepsis, NEC and other comorbidities while this increases the probability of developing RDS.[38 42]

This study revealed that multiple pregnancy was an independent predictor of RDS. This finding is supported by a study conducted in China,[51] the reason for this occurrence is due increased risk of preterm labour and preterm birth in multiple births, and the neonate delivered before their organ systems become completely matured.[52] The other possible justification is multiple neonates have a higher risk of getting congenital anomalies and IUGR, which increases the risk of RDS.[42]

The current study found that a low APGAR score <7 at the fifth minute is an independent predictor of RDS among LBW neonates. This finding is supported by different studies conducted in China,[53] Indonesia[54] and Saudi Arabia.[2] The possible reason for this is a low APGAR score, which is defined as asphyxia, and asphyxia at birth can cause direct harm to alveolar type II epithelial cells and impair the generation of surfactant, which will raise the incidence of RDS. Additionally, the following two factors are the other reasons for this: hypoxia decreases pulmonary surfactant activity and may even lead to its inactivation, whereas severe birth asphyxia diminishes pulmonary surfactant synthesis and secretion.[27]

Being born extremely very low and very LBW increases the hazard of RDS among LBW neonates. This finding is supported by different studies conducted in China,[49] Indonesia,[54] Vietnam[55] and Saudi Arabia.[2] The possible justification for this is a lack of surfactant caused by lung immaturity is one example of the physiological and anatomical immaturities that can occur in newborns who have LBW.[56] The other reason is as birth weight decreases the risk of exposure/ vulnerability to various medical problems such as hypoglycaemia, sepsis and cold stress increases.[33 42] Hence, these medical problems individually, or simultaneously, increase the risk of developing RDS.[42] The present study has the following limitations: due to its retrospective nature, some important variables, such as maternal nutritional status, family income and educational level, were missed. In addition, the hospital's service context and supplies were not assessed.

Conclusion

The current study showed that the incidence of RDS was higher than other studies conducted on other groups of neonates. A high incidence rate was seen among extremely LBW and very LBW neonates. Fifth minute APGAR score, caesarian section, multiple births, prematurity, extremely LBW and very LBW were significant predictors of RDS. Hence, healthcare providers and other concerned stakeholders should give due attention, and appropriate intervention for LBW neonates with the aforementioned preventable and treatable factors. Furthermore, a prospective follow-up study needs to be conducted to assess the true association of predictors.

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