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Research article

Incidence and predictors of neonatal seizures among neonates admitted in Debre Markos Comprehensive Specialized Hospital, Northwest Ethiopia. A prospective follow-up study

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ABSTRACT

Introduction: Neonatal seizures are the most common neurological problem among newborns. To date, scientific studies on the incidence and predictors of neonatal seizures in African countries, including Ethiopia are scarce. Therefore, this study aimed to assess the incidence and predictors of neonatal seizures among neonates admitted to Debre Markos comprehensive Specialized Hospital.

Methods: An institutional-based prospective follow-up study was conducted i**n** Debre Markos comprehensive specialized hospital from February 1**,** 2022 to January 30, 2023. A systematic random sampling technique was used to select a total of 198 neonates. Data were entered into Epi-Data 4.2 and then exported to STATA version 14.1 for analysis. The Kaplan-Meier survival curve and the log-rank test were computed to explore the descriptive statistics. Variables with a p-value $\leq$0.2 in bi-variable Cox-regression were selected for multivariable Cox-regression analysis. Finally, a p-value of $<$0.05 was used to declare the statistical significance of the association with the outcome variable.

Results: The overall incidence rate of neonatal seizures was 35 per 1000 person-day observations. The mean follow-up time for this study was 123.4 h. The cumulative survival probability of neonates' at 0 to 24 and 0–72 h was 89.8 % and 81.71 %, respectively. The statistically significant predictors for the incidence of neonatal seizures were perinatal asphyxia (AHR = 10.95; 95%CI: 4.81, 24.93), subgaleal hemorrhage (AHR = 5.17; 95%CI: 2.09, 12.79), and gestational age $<$37 weeks (AHR = 4.62; 95%CI: 1.62, 13.22).

Conclusions: The incidence rate of neonatal seizures in this study was high. Neonates born with gestational age $<$37 weeks, having perinatal asphyxia, and having subgaleal hemorrhage were statistical predictors for the incidence of neonatal seizures. Thus, healthcare professionals should

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give special attention to neonates born with gestational age <37 weeks, prevent perinatal asphyxia and subgaleal hemorrhage.

1. Introduction

The neonatal period is a time of intense brain development, cortical lamination, neurite outgrowth, synaptogenesis, and the elementary stages of brain myelination [1]. Neonatal seizures is a paroxysmal alteration in neurological functions like motor, behavior and autonomic functions of the body, and it is the most common neurological disorder in the neonatal period [2,3]. Neonatal seizures often indicate an underlying neurologic disturbance; they require an immediate medical assessment to determine the underlying cause and necessary interventions [4].

Seizures is more common in the neonatal period than in any other stage of life, affecting approximately 5 % of all neonates [5]. It is evidenced by rapid eye movements, abnormal movements of the limbs, skin mottling or cyanosis, autonomic phenomena, or any loss of consciousness or sleeping that needs to be elicited. Birth asphyxia is the commonest cause of neonatal seizures, while other causes include septicemia with or without central nervous system infection, transient metabolic disorder, and intracranial bleeding [6,7].

Globally, the incidence of neonatal seizures account for 5 per 1000 live births and is common in preterm infants, ranging from 19 to 57.5 per 1000 live births [8,9]. About 25–55 % of neonatal seizures cases occur in the first 24 h of life [10]. Half of neonatal seizures cases will develop epilepsy later in life; 32.1 % developed neurological complications; and 18.35 % died due to seizures [4]. The parents of the neonates with neonatal seizures develop anxiety and depression, which leads to poor parental quality of life [11].

According to various studies conducted around the globe, age of neonate, birth weight, sex of neonate, maternal diabetes, pre-eclampsia, obesity, smoking, cerebral malformations, and metabolic disturbances are all significant risk factors for the development of neonatal seizures [12–15].

Despite neonatal seizures is considered a major public health problem in the world, particularly in African countries [16–18], as far as authors search of literatures, there is a scarcity of studies on the incidence and predictors of neonatal seizures in Ethiopia. Therefore, this study aimed to assess the incidence and predictors of neonatal seizures among neonates admitted to Debre Markos comprehensive specialized hospital.

2. Methods

2.1. Study settings

Institution-based prospective follow-up study was conducted from February 1, 2022, to January 30, 2023**,** among neonates aged between 0 and 28 days.

This study was conducted at Debre Markos comprehensive specialized hospital, which is located at Debre Markos town. Debre Markos town is 300 km far from Addis Ababa, the capital city of Ethiopia, and 265 km from Bahir-dar, the capital city of the Amhara region. The town has a total population of 262,497, of whom 129,921 are men and 132,576 women. Currently, Debre Markos town has one comprehensive specialized hospital, three government health centers, and eight private specialty clinics. The hospital serves about 5 million people in the East Gojjam Zone and neighboring zones. The Neonatal Intensive Care Unit (NICU) admits around 2550 neonates per year, and monthly average admissions were 225. The NICU has a total of 46 beds for neonatal admission, Kangaroo Mother Care (KMC), and a maternity waiting room. Nurses, general practitioners, senior physicians, and other supporting staffs are working in the NICU.

2.2. Population and eligibility criteria

All neonates who were admitted to the NICU in Debre Markos comprehensive specialized hospital were the source population, and the study population were neonates who were admitted to the NICU during the study period.

Neonates aged between 0 and 28 days and admitted to the NICU from January 11, 2022, to February 30, 2023, were included, whereas those neonates who had uncertain clinical manifestations like jitteriness, tetanic spasms, complex malformations, and neonates having seizures during admission were excluded.

2.3. Sample size and sampling procedures

The sample size was calculated by using the general formula for sample size calculation for time-to-event data. Using the Stata 14.1 software for power and sample size calculation by considering the “survival probability (0.5), power (0.8), value of p at 95 % confidence level (1.96), hazard ratio (0.5), and withdrawal probability (0.1)”. Therefore, the final sample size for this study was 198. The study participants were selected using a systematic random sampling technique from the neonatal registration logbook. Neonates were selected in every ninth interval (K = 9) until the required sample size was fulfilled.

2.4. Variables

Dependent variable: Incidence of neonatal seizure.

Independent variables:

Socio demographic variables: Maternal age, age of neonate, sex of neonate, residency, occupation of the mother and educational level of the mother.

Obstetrics and gynecologic related variables: parity, gravidity, type of pregnancy, antenatal care follow up (ANC), place of delivery, mode of delivery, duration of labor, mothers' chronic medical illness, and family history of seizures.

Neonatal related variables: baseline vital sign of the neonate, gestational age at birth, feeding status, treatment given during NICU stay, medical diagnosis at admission and condition of the neonate at discharge.

2.5. Operational definitions

Event: Neonates who develop a seizure according to the WHO guidelines and physician diagnosis within the follow-up period.

Censored: Neonates who didn't develop an event during the follow-up period, had death, and were left against medical advice, transferred out, or referred before the development of an event.

Follow-up period: The time interval from admission to the NICU to the occurrence of an event or censorship.

Survival time: Length of time in hours followed from admission of the neonate to the development of neonatal seizures.

Neonatal seizures: Neonates who develop a seizures according to the physician's decision based on WHO guideline.

Neonatal period: Begins at birth and ends at 28 completed days of life [19].

2.6. Data collection tool and procedures

The data collection tool was developed after reviewing different related literatures [4,20–27]. The tool included potential predictor variables, such as socio-demographic, maternal, neonatal-related characteristics of the study participants. The questionnaire was prepared in English-language.

After the preparation of a structured data collection tool, two data collectors and one supervisor were assigned. Baseline information was collected immediately after admission to the NCU from the neonatal registration book, neonatal chart, and maternal registration book. In addition, all relevant data were collected throughout the follow-up period in daily basis.

2.7. Data quality control

To ensure the quality of the data, a pretest was done among 10 neonates who were admitted to Lumamie hospital before starting the actual data collection process. Moreover, a one-day training was given to data collectors and supervisor. The data were checked for consistency and completeness. Strict follow-up and supervision were carried out during the data collection period. The reliability of the tool was checked using Cronbach's alpha and it was 0.79.

2.8. Data processing and analysis

The data were entered into Epi-Data 4.2 and then exported to STATA version 14.1 for further coding, cleaning, and analysis. Depending on the nature of the data, descriptive statistics such as mean with standard deviation, median with interquartile range, and frequencies with percentages were used to describe the characteristics of the study participants. Moreover, the results were presented

Table 1
Baseline Socio-demographic-related characteristics of study participants in Debre Markos comprehensive specialized Hospital, Northwest Ethiopia, 2023.

Variables	Category	Number (%)	Neonatal seizures status	
			Event (%)	Censored (%)
Maternal age	<35 years	145 (73.23 %)	31 (86.12 %)	114 (70.4 %)
	≥35 years	53 (26.77 %)	5 (13.88 %)	48 (29.6 %)
Age of neonate in hours	<24	121 (61.1 %)	21 (58.33 %)	100 (61.72 %)
	25–168	59 (29.8 %)	13 (36.11 %)	46 (28.39 %)
	≥169	18 (9.09 %)	2 (5.55 %)	16 (9.87 %)
Sex of neonate	Male	125 (63.13 %)	24 (66.66 %)	101 (62.34 %)
	Female	73 (36.87 %)	12 (33.34 %)	61 (37.66 %)
Residence	Urban	95 (47.98 %)	18 (50 %)	77 (47.53 %)
	Rural	103 (52.02 %)	18 (50 %)	85 (52.47 %)
Occupation of the mother	Employed	73 (36.8 %)	16 (44.4 %)	57 (35.18 %)
	Unemployed	125 (63.2 %)	20 (55.6 %)	105 (64.82 %)
Educational status of the mother	Illiterate	86 (43.43 %)	19 (52.77 %)	67 (41.35 %)
	Literate	112 (56.57 %)	17 (47.23 %)	95 (58.65 %)

using texts, tables, and graphs. The Kaplan-Meier survival curve, together with the log-rank test, was used to assess the cumulative probability and survival difference between groups. A bi-variable Cox-proportional hazards regression analysis was conducted for each independent variable. Variables with a p-value ≤0.2 were candidates for the multivariable Cox-proportional hazards regression analysis. An Adjusted Hazard Ratio (AHR) with 95 % confidence intervals (CI) was used to report the strength of association between the predictor variables and the incidence of neonatal seizures. Statistical significance was declared when the p-value was less than 0.05. The Cox-proportional hazard model assumptions were checked by using the Schoenfeld residuals statistical test (global test), and it was 0.3783. The model's fitness was assessed using the Cox-Snell residuals graph.

3. Results

3.1. Baseline socio-demographic-related characteristics of participants

A total of 198 neonates were enrolled in this study during the study period. This study found that the mean age of neonates and mothers was 61.6 h and 29.9 years, respectively. Among the total study participants, 125 (63.1 %) were males and 103 (52.02 %) were come from rural areas. More than half of (57.07 %) the neonates' mothers were aged less than 35 years. Moreover, about 73 (36.8 %) of neonates' mothers were employed, and 112 (56.57 %) were literate (Table 1).

3.2. Maternal-related characteristics of the study participants

The majority of (90.4 %) neonates' mothers had at least one ANC follow-up, and nearly all 195 (98.5 %) were delivered at a health institution. Three-fourths of (75.76 %) mothers were delivered by Spontaneous Vaginal Delivery (SVD). Regarding the duration of labour, nearly one-fourth (21.72 %) of mothers had prolonged labour (Table 2).

3.3. Maternal medical illness-related characteristics

Among 198 neonates' mothers, only 1 mother had DM and HIV, respectively. Similarly, only two mothers have HIV infection among 198 mother-neonate pairs.

3.4. Neonatal-related characteristics

Among 198 neonates, 25 (13.1 %) had an APGAR score of 0–3. About 192 (96.97 %) neonates were fed exclusive breast-feeding. Regarding the reason for admission, two-thirds (66.67 %) of neonates were admitted due to PNA, followed by neonatal sepsis (19.44 %) (Table 3).

Table 2
Maternal-related characteristics of study participants in Debre Markos comprehensive specialized hospital, Northwest Ethiopia, 2023.

Variables	Category	Number (%)	Neonatal seizures status	
			Event (%)	Censored (%)
Parity	Primipara	150 (75.76 %)	10 (27.78 %)	44 (27.16 %)
	Multipara	20 (10.1 %)	21 (58.33 %)	102 (62.96 %)
	Grand-multipara	28 (14.14 %)	5 (13.89 %)	16 (9.88 %)
Birth type	Singleton	175 (88.38 %)	33 (91.67 %)	142 (87.65 %)
	Twin and more	23 (11.62 %)	3 (8.33 %)	20 (12.35 %)
ANC* visit	Yes	179 (90.4 %)	34 (94.44 %)	145 (89.51 %)
	No	19 (9.6 %)	2 (5.56 %)	17 (10.49 %)
Place of delivery	Institution	182 (91.92 %)	35 (97.23 %)	147 (89.51 %)
	Home	16 (8.08 %)	1 (2.77 %)	15 (10.49 %)
Mode of delivery	SVD*	150 (75.76 %)	22 (61.11 %)	128 (79.01 %)
	Instrumental	20 (10.1 %)	6 (16.67 %)	14 (8.64 %)
	C/S*	28 (14.14 %)	8 (22.22 %)	20 (12.35 %)
Maternal eclampsia	Yes	15 (7.58 %)	5 (13.88 %)	10 (6.17 %)
	No	183 (92.42 %)	31 (86.11 %)	152 (93.83 %)
PROM*	Yes	2 (1.01 %)	2 (5.56 %)	2 (1.23 %)
	No	196 (98.97 %)	34 (94.44 %)	160 (98.77 %)
Prolonged labour	Yes	43 (21.72 %)	16 (44.55 %)	27 (16.66 %)
	No	155 (78.28 %)	20 (55.5 %)	135 (83.34 %)
Obstructed labour	Yes	239 (11.6 %)	6 (16.66 %)	17 (10.49 %)
	No	175 (88.4 %)	30 (83.34 %)	145 (89.51 %)
Post-partum hemorrhage	Yes	4 (2.02 %)	1 (2.77 %)	3 (1.85 %)
	No	194 (97.98 %)	35 (97.22 %)	159 (98.15 %)
Nutritional status	Malnourished	66 (33.33 %)	13 (36.11 %)	53 (32.7 %)
	Well-nourished	132 (66.67 %)	23 (63.89 %)	109 (67.3 %)

ANC; Antenatal Care, C/S; Cesarean Section, PROM; Premature Rapture Of Membrane, SVD; Spontaneous Vaginal Delivery.

Table 3
Neonatal-related characteristics of study participants in Debre Markos comprehensive specialized hospital, Northwest Ethiopia, 2023.

Variables	Category	Number (%)	Neonatal seizures status	
			Event (%)	Censored (%)
Birth weight	Low	129 (65.15 %)	11 (30.55 %)	118 (72.83 %)
	Normal	65 (32.82 %)	23 (63.89 %)	42 (25.92 %)
	Overweight	4 (3.12 %)	2 (2.77 %)	22 (1.23 %)
Feeding type	Exclusive breast feeding	192 (96.97 %)	36 (100 %)	156 (96.3 %)
	Mixed feeding	6 (3.03 %)	0	6 (3.7 %)
APGAR* score	0–3	26 (13.13 %)	8 (22.22 %)	18 (11.11 %)
	4–6	128 (64.65 %)	23 (63.88 %)	105 (64.81 %)
	7–10	44 (22.22 %)	5 (13.88 %)	39 (24.07 %)
Temperature in ^{0}c	≤36.4	130 (65.65 %)	24 (66.66 %)	106 (65.43 %)
	36.5–37.5	47 (23.73 %)	9 (25 %)	38 (23.45 %)
	≥37.6	21 (10.60 %)	3 (8.33 %)	18 (11.11 %)
Pulse rate (beat/minute)	<100	8 (4.04 %)	2 (5.55 %)	6 (3.7 %)
	100–150	137 (69.19 %)	24 (66.67 %)	113 (69.75 %)
	>150	53 (26.76 %)	10 (27.77 %)	43 (26.54 %)
Respiratory rate (breath/minute)	<50	81 (40.90 %)	13 (36.11 %)	68 (41.97 %)
	50–60	60 (37.03 %)	12 (33.33 %)	48 (29.62 %)
	>60	57 (35.18 %)	11 (30.55 %)	46 (28.39 %)
Oxygen saturation	<95 %	125 (63.13 %)	27 (75 %)	98 (60.49 %)
	>95 %	73 (36.87 %)	9 (25 %)	64 (39.5 %)
Random blood sugar (mg/dl)	<45	9 (4.54 %)	2 (5.55 %)	7 (4.32 %)
	45–126	158 (79.79 %)	24 (66.67 %)	134 (82.71 %)
	>126	31 (15.65 %)	10 (27.77 %)	21 (12.96 %)
PNA*	Yes	38 (19.19 %)	27 (75 %)	11 (6.79 %)
	No	160 (80.8 %)	9 (25 %)	151 (93.21 %)
ARDS*	Yes	23 (11.62 %)	4 (11.11 %)	19 (11.73 %)
	No	175 (88.38 %)	32 (88.89 %)	143 (88.27 %)
Neonatal sepsis	Yes	107 (54.04 %)	21 (58.33 %)	86 (53.08 %)
	No	91 (45.96 %)	15 (41.67 %)	76 (46.92 %)
Hypothermia	Yes	66 (33.33 %)	21 (58.33 %)	51 (31.48 %)
	N o	132 (66.67 %)	15 (41.67 %)	111 (68.52 %)
Pre term	Yes	51 (25.75 %)	4 (11.11 %)	47 (29.01 %)
	No	147 (74.25 %)	32 (88.89 %)	115 (70.99 %)
Low birth weight	Yes	88 (44.44 %)	10 (27.77 %)	78 (8.14 %)
	No	110 (55.56 %)	26 (72.23 %)	84 (51.86 %)
Hypoglycemia	Yes	26 (13.13 %)	7 (19.44 %)	19 (11.73 %)
	No	172 (86.87 %)	29 (80.56 %)	143 (88.27)
Neonatal jaundice	Yes	20 (10.1 %)	6 (16.66 %)	14 (8.64 %)
	No	178 (89.89 %)	30 (83.33 %)	148 (91.35 %)
Subgaleal hemorrhage	Yes	17 (8.58 %)	8 (22.22 %)	9 (5.55 %)
	No	181 (91.41 %)	28 (77.78 %)	153 (94.45 %)
Types of seizures	Subtle		7 (19.44 %)	
	Tonic		24 (66.67 %)	
	Clonic		3 (8.33 %)	
	Myoclonic		2 (5.55 %)	

Footnote: *PNA-Perinatal Asphyxia, ARDS- Acute Respiratory Distress Syndrome.

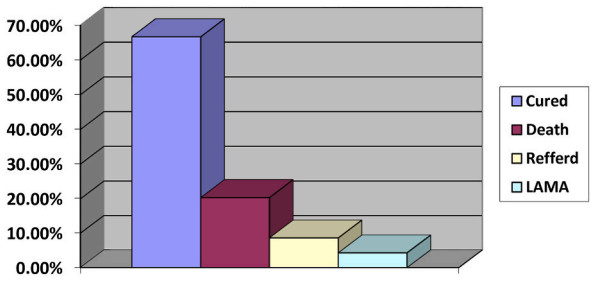

Fig. 1. Outcomes of neonates admitted to the NICU in Debre Markos comprehensive specialized hospital, 2023.

3.5. Outcomes of neonates

Out of 162 neonates censored, 108 (66.66 %) were cured and 33 (20.37) were died (Fig. 1).

3.6. Incidence of neonatal seizures

During the follow-up period, a total of 36 neonates developed neonatal seizures making the Incidence Rate (IR) 35 per 1000 person-day observations. The total follow-up risk time was 1017.95 days, with a minimum of 1 h and a maximum of 670 h.

According to the Kaplan-Meier estimate curve cumulative probability of neonatal seizures was 76.22 % (Fig. 2).

The life table shows that the cumulative probability of survival with time intervals of 0–24 h, 25–48 h, and 49–72 h was 89 %, 85 %, and 82 %, respectively (Table 4).

3.7. Predictors of neonatal seizures

Based on the bi-variable cox-regression analysis, perinatal asphyxia, gestational age, mode of delivery, subgaleal hemorrhage, prolonged labour, birth weight, place of delivery, APGAR score, and eclampsia were selected for the multi-variable cox-regression analysis. Subsequently, a multi-variable cox-regression analysis was employed. Finally, three variables were found to be statistically significant predictors of the incidence of neonatal seizures.

The hazard of developing neonatal seizures among neonates who had perinatal asphyxia was 11 times (AHR = 10.95, 95%CI: 4.81, 24.93) higher than their counterparts. Those neonates who had subgaleal hemorrhage were five times (AHR = 5.17, 95%CI: 2.09, 12.79) more likely to develop neonatal seizures compared to those who hadn't had subgaleal hemorrhage. Furthermore, the hazard of developing neonatal seizures among preterm neonates was 4.6 times (AHR = 4.62, 95%CI: 1.62, 13.22) higher than that of term neonates (Table 5).

3.8. Model goodness of fit test

The Cox-Snell residuals have been employed to check the goodness of fit test. The model was found to be well-fitted when the hazard function approaches the baseline hazard about 45°. It was possible to infer from the residual test that the final model provided a good fit for the data (Fig. 3).

4. Discussion

Neonatal seizures are frequently encountered neurological problem in the neonatals which leads to increased long-term morbidity and mortality. It is also considered a major public health threat due to its risk for neonatal death, and survivors may develop neurological disability later in life.

This prospective follow-up study found that the incidence rate of neonatal seizures was 35 per 1000 person-day observations (95 % CI: 23.1, 39.4). This finding was higher than the studies conducted in Sweden, Italy, and UK, which reported that the overall incidence of neonatal seizures was 2.1, 1.5, 1.5–5.5 per 1000 live births, respectively [12,28,29]. Moreover, this finding is also higher than the study conducted in Pakistan that showed that the incidence of neonatal seizures ranged from 0.1 to 0.5 per 100 live births in term neonates [30]. This discrepancy might be due to the difference in the study setting, level of NICU, availability of advanced neuro-imaging facilities, including EEG machine, and quality of service provided [31,32]. The study conducted in Ethiopia found that

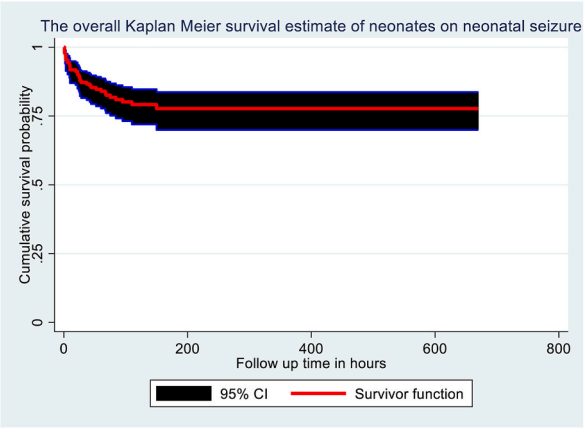

Fig. 2. The KM survival estimate to describe the cumulative probability of neonatal seizures during follow up time in Debre Markos comprehensive specialized hospital, Northwest Ethiopia, 2023.

Table 4
Life table for the incidence of neonatal seizures among neonates admitted to Debre Markos comprehensive specialized hospital, Northwest Ethiopia 2023.

Life table with 24 h' time interval category						
Time interval in hours	Total number of neonates	Number events	Censored	Probability Survival	Std. Error	[95 % Conf. Interval.]
0–24	198	19	22	0.89	0.02	0.84–0.93
25–48	157	8	17	0.85	0.03	0.78–0.89
49–72	132	4	18	0.82	0.03	0.75–0.87
Life table with 72 h' time interval category						
0–72	198	31	57	0.81	0.03	0.75–0.86
73–144	110	4	46	0.77	0.03	0.70–0.83
145–216	60	1	30	0.76	0.03	0.67–0.82
217–288	29	0	9	0.76	0.04	0.67–0.82
288–360	20	0	4	0.76	0.04	0.67–0.82
360–432	16	0	6	0.76	0.04	0.67–0.82
432–504	10	0	4	0.76	0.04	0.67–0.82

Table 5
Bi-variable and multi-variable Cox-regression analysis for predictors of neonatal seizures among neonates admitted to Debre Markos comprehensive specialized hospital, Northwest Ethiopia, 2023.

Variables name	Category	Censored	Event	CHR (with 95 % CI)	AHR (with 95 % CI)	*P*-value
Mode of delivery	SVD	128	22	1	1	
	C/S	14	6	2.34 (0.95, 5.79)	0.67 (0.57, 3.12)	0.06
	Instrumental	20	8	2.26 (1.00,5.10)	0.46 (0.12,1.67)	0.33
Maternal complication	No	120	15	1	1	
	Yes	42	21	0.28 (0.14,0.54)	0.53 (0.14, 2.03)	0.36
Eclampsia	No	152	31	1	1	
	Yes	10	5	0.46 (0.17,1.18)	0.71 (0.18, 2.72)	0.62
Prolonged labour	No	135	20	1	1	
	Yes	27	16	0.28 (0.14, 0.55)	0.61 (0.16, 2.23)	0.46
APGAR score at 10 min	≥7	39	5	1	1	
	4–6	105	23	0.47 (0.21, 1.06)	1.93 (0.63, 5.85)	0.24
	<3	18	8	0.27 (0.08, 0.84)	0.77 (0.21, 2.79)	0.693
Gestational age	>37 weeks	115	27	1	1	
	<37 weeks	47	11	4.4 (2.17, 9.0)	4.6 (1.6, 13.21)	**0.008***
PNA	No	151	27	1	1	
	Yes	11	9	17.52 (8.36, 36.72)	10.95 (4.81, 24.93)	< **0.001****
Duration of labour	<12 h	135	21	1	1	
	>12 h	27	15	0.28 (0.14, 0.55)	0.61 (0.16, 2.23)	0.460
subgaleal hemorrhage	No	148	25	1	1	
	Yes	14	11	5.55 (2.71, 11.34)	5.17 (2.09, 12.79)	**0.001***
Place of delivery	Institution	153	32	1	1	
	Home	9	4	3.65 (0.50, 6.67)	1.72 (0.19, 15.94)	0.630

CHR-crude hazard ratio, **AHR**-adjusted hazard ratio and **CI** -confidence interval.

the incidence of neonatal seizures was found 13.6 per 1000 live births which is higher than the current study [33].

However, this finding is lower than the studies conducted in Pakistan, which found that the incidence of neonatal seizures was 57.5 per 1000 live births [5]. This might be due to differences in the study population, follow-up period, and study settings. The higher number of term neonates included in this study might lower the incidence of neonatal seizures. It is a well-documented fact that the incidence of neonatal seizures is high among pre-term neonates [8,10,14,21,24].

This study found that the presence of perinatal asphyxia, subgaleal hemorrhage, and being preterm were independent predictors for the incidence of neonatal seizures according to the multivariable Cox-proportional hazard regression model analysis.

The hazard of developing neonatal seizures among neonates who had perinatal asphyxia was 11 times higher compared with those who hadn't had perinatal asphyxia. This finding was supported by other studies conducted in Sweden, USA, and India [34–36]. It has been well known that perinatal asphyxia is an important cause of Hypoxic Ischemic Encephalopathy (HIE), which leads to hyper-excitability of the brain due to the interplay between a high density synaptic network and paradoxical excitatory actions of primary inhibitory networks [37,38].

The hazard of developing neonatal seizures among neonates with subgaleal hemorrhage was five times higher compared with their counterparts. The study carried out in India provides support for this finding [14]. This could be explained by the scientific evidence that subgaleal hemorrhage occurs in the loose connective tissue within the subgaleal space, which leads to hypovolemia and HIE [39].

Additionally, this study found a significant association between the incidence of neonatal seizures and preterm delivery. The hazard of evolving neonatal seizures among preterm neonates was 4.6 times higher compared with term neonates. This finding was consistent with other similar studies conducted in Italy, Sweden, Pakistan, and Ethiopia [17,31–33]. This could be explained by the scientific evidence that in preterm neonates premyelinating oligodendrocyte progenitor cells are particularly vulnerable to HIE due to immature

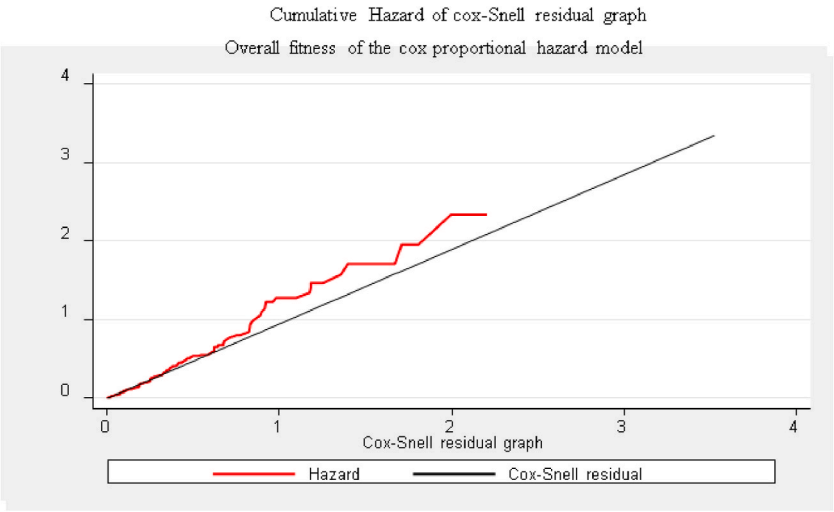

Fig. 3. Cox-Snell residual graph to check the model fitness to assess incidence of neonatal seizures among neonates admitted to Debre Markos comprehensive specialized hospital, Northwest Ethiopia, 2023.

blood flow, auto-regulation, and inadequate cardiac output, which in turn leads to neonatal seizures [40,41]. Moreover, being preterm is associated with reduced cerebral and cerebellar volumes, diminished cortical gyrification, and delayed maturation of white and gray matter of neuronal structures [42].

4.1. Limitations of the study

This study has some limitations. Since there was no standardized diagnostic approach, like an EEG, to establish the diagnosis, the physician's judgment was used, which may not be deemed reliable. Furthermore, the sample size for the current study was relatively small, which possibly reduced the power of the study. Hence, this study only included admitted neonates at hospital level, it may not be generalized to all neonates.

5. Conclusion

This study found that the incidence density rate of neonatal seizures was high. The presence of perinatal asphyxia, subgaleal hemorrhage, and being preterm were significant predictors for the incidence of neonatal seizures. It is better to strengthen ANC follow-up and skilled delivery services to decrease the occurrence of perinatal asphyxia, subgaleal hemorrhage and preterm births. Further studies with a longer follow-up period and a larger sample size are warranted.

Ethical approval and consent to participate

The study was approved by Ethical Review Committee of Debre Markos University with the reference number HSC/R/C/Ser/PG/Co/58/11/14. Based on the declaration of Helsinki, informed assent from the mothers was obtained. Data was kept anonymously by coding to keep confidentiality. All the processes of the research were performed and secured in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

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Data availability statement

All data is available within the manuscript and supportive materials.

CRediT authorship contribution statement

Tefera Alemayehu: Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Tsige Gebre:** Writing – review & editing, Visualization, Validation, Supervision, Software, Methodology. **Bayachew Asmare:** Writing – review & editing, Supervision, Software, Investigation. **Yilkal Tafere:** Writing – review & editing, Visualization, Validation, Supervision, Data curation. **Bekalu Kassie:** Writing – review & editing, Visualization, Validation, Supervision, Methodology. **Tilahun Degu Tsega:** Writing – review & editing, Supervision, Software, Methodology, Conceptualization. **Mulu Alemu:** Writing – review & editing, Validation, Resources, Investigation, Data curation, Conceptualization. **Mengistu Abebe Messelu:** Writing – review & editing, Visualization, Validation, Supervision, Software, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations and acronyms

AHR	Adjusted Hazard Ratio
ANC	Antenatal Care
CHR	Crude Hazard Ratio
CI	Confidence interval
CNS	Central Nervous System
EEG	Electroencephalogram
GA	Gestational Age
HIE	Hypoxic Ischemic Encephalopathy
IQR	Inter quartile Range
NICU	Neonatal intensive care unit
PNA	Prenatal asphyxia
SVD	Spontaneous vaginal delivery
WHO	World Health Organization

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e29999.

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