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Predictors of mortality in the neonatal intensive care unit of El-Galaa Teaching Hospital

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Abstract

Aim
Neonatal mortality accounts for most infant mortality. Various factors influence the risk of neonatal mortality. Available estimates of survival and mortality in neonatal intensive care units (NICUs) are needed to provide antenatal counseling and guide management decisions. This study aimed to determine the predictors of admitted neonatal mortality.

Patients and methods
A retrospective study was done between June 2016 and May 2018 in the NICU of El-Galaa Teaching Hospital to determine the predictors of admitted neonatal mortality. Data were collected as follows: premature rupture of membranes, mode of delivery, multiple or single pregnancy, sex, weight, gestational age (GA), Apgar score at 5 min, mechanical ventilation use, presence of hemorrhage during the course of treatment, central nervous system (CNS) problems, pneumothorax, and neonatal sepsis. Univariate analysis and logistic regression analysis were done to determine the predictors of mortality.

Results
A total of 987 neonates were enrolled in this study. Nonsurvivors represented 41.9%, whereas survivors represented 58.1%. Results show a statistically significant difference of more deaths with multiple pregnancy, vaginal delivery, mechanical ventilation, sepsis, pneumothorax, CNS problems, hemorrhage, low GA, low birth weight, low Apgar score at 5 min, and low days of NICU admission. Findings from bivariate analysis showed that hemorrhage, mechanical ventilation, pneumothorax, CNS problems, vaginal delivery, and sepsis were significantly associated with less time to death. Cox regression analysis and odd ratio showed that hemorrhage, sepsis, and pneumothorax have the most effect on mortality, whereas high GA and high Apgar score at 5 min are significant to survival.

Conclusions
The study revealed that most NICU deaths occurred in the first week and showed that hemorrhage, sepsis, and pneumothorax have the most effect on mortality, whereas higher GA and higher Apgar score at 5 min to survival.

Keywords: Neonatal mortality, neonatal intensive care unit, prediction

Introduction

There are ~ 3 million neonatal deaths in the first 28 days of life per year worldwide [1]. Nearly all (99%) of them occur in low-income and middle-income countries [2]. Preterms account for many of these deaths and more than 60% of them occur in Africa and South Asia. Egypt is one of the ten countries with the largest number of preterm births [3]. Many tools to assess and predict neonatal mortality risk have been developed to overcome the problems of varied causes of neonatal mortality and different risk factors that predispose to it [4]. Available estimates of survival and mortality of neonates in neonatal intensive care unit (NICU) are needed for neonatologists to provide antenatal counselling to parents and guide management decisions [5]. The advantage of prediction models is that they combine risk factors, allowing

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more accurate risk estimation [6], which is also correlated with provision of appropriate patient care and management of medical resources [7]. It can be used also to stratify patients in the arms of clinical trials or for comparing quality improvement efforts in different populations [8]. Neonatal mortality prediction models are widely applied in high-income countries, which account for only 1% of neonatal deaths [9]. Application of a prediction model in the setting can be done by using an existing model, remodeling and validating an existing model, or creating a new one [10]. This study was designed to determine the predictors of admitted neonatal mortality.

Patients and methods

A retrospective study was done between June 2016 and May 2018 in the NICU of EL-Galaa Teaching Hospital to estimate the time to death and predictors of admitted neonatal mortality. The hospital serves as both comprehensive and referral level care unit. The department has 1:5 nurse-patient ratio and 1:10 doctor-patient ratio for 24 h and seven days with total of 30 neonatal beds. It provides an outpatient and inpatient medical service for neonates free of charge. Inclusion criteria were all neonates of both sexes admitted to the NICU after stabilization of the neonates after the first 24 h. Exclusion criteria were first, neonates weighing less than 700 g and with gestational age (GA) less than 26 weeks; second, presence of lethal congenital malformations; third, death or discharge in the delivery room or within 24 h of life; and fourth, surgical emergencies.

Data collection

The data were extracted using a structured form, which was prepared by the author. Residents had collected the data from medical records of the neonates. The form comprised obstetric data, such as premature rupture of membranes (PROM) greater than 18 h before delivery, mode of delivery (vaginal or cesarean), and multiple or single pregnancy; neonatal data, such as sex of the neonate (male or female), weight in grams using an electronic scale, GA estimated by New Ballard Score, and Apgar score at 5 min; and progression data, such as use of mechanical ventilation during the course of treatment, presence of hemorrhage evidenced clinically (gastrointestinal or pulmonary) or by cranial ultrasound, presence of central nervous system (CNS) problems (convulsions and hypoxia evidenced by cranial ultrasound), occurrence of pneumothorax (evidenced by radiography), and occurrence of neonatal sepsis (evidenced by blood culture). The research consent from parents or guardians for enrolment of their neonate in the study was taken individually. Survival was defined as the proportion of live births surviving up to the time of discharge. The outcome measure was in-hospital death. Univariate analysis and logistic regression analysis were done to determine the predictors of mortality.

Statistical methods

Data were collected and entered using the statistical package SPSS 21 SPSS, V.21 software (IBM Corp., Armonk, New York, USA). Data were summarized using number and percentage for qualitative variables, mean and SD for quantitative variables which are normally distributed, whereas median and interquartile range used for quantitative variables that are not normally distributed. Comparison between groups was done using χ^2-test for qualitative variables, whereas nonparametric Mann–Whitney test was used for quantitative variables that are not normally distributed. The Kaplan–Meier method was calculated to estimate mortality rate of neonates. The effect of GA, birth weight, neonatal sex, and Apgar score on survival were studied by Kaplan–Meier survival estimators for each category using log rank test. Cox regression analysis was done to test for predictors of neonatal survive and predicted probability score was analyzed using recessive operator characteristic (ROC) curve. *P* values less than or equal to 0.05 were considered as statistically significant.

Results

A total of 987 neonates were enrolled in this retrospective study done between June 2016 and May 2018 in the NICU of El-Galaa Teaching Hospital. Nonsurvivors represented 414 (41.9%), whereas survivors represented 573 (58.1%). Overall, 53% of deaths were in the first week (excluding deaths in first 24 h) and 25% of deaths were in the second week. The descriptive data of the neonates are presented in Tables 1 and 2. It shows a statistically significant difference, with more deaths with multiple pregnancy, vaginal delivery, mechanical ventilation, presence of sepsis, pneumothorax, CNS problems, hemorrhage, low GA, low birth weight, low Apgar score at 5 min, and low days of NICU admission, whereas there was no significant statistical difference concerning sex or PROM.

Findings from bivariate analysis showed that hemorrhage, mechanical ventilation, pneumothorax, CNS problems, vaginal delivery, and sepsis were significantly associated with less time to death of neonates (arranged from less to more), whereas there was no statistical significant difference concerning multiple pregnancy, sex, or PROM (Table 3 and Figs. 1–5).

By Cox regression analysis of factors studied before NICU admission (multiple pregnancy, mode of delivery, weight, GA, and Apgar score at 5 min), ROC curve was not statistically significant (Tables 4,5 and Fig. 6)

With Cox regression analysis of the factors studied after NICU admission during the treatment course (sepsis, CNS problems, hemorrhage, and pneumothorax), ROC curve shows statistically significant results (Table 4 and Fig. 7), with area under the curve of 0.628 [95% confidence interval (CI): 0.637–0.728; $P < 0.001$]. The factors that showed statistical significant predictors of mortality are presence of sepsis ($P < 0.001$; odds ratio (OR): 1.596; 95%CI: 1.245–2.05), hemorrhage ($P < 0.001$; OR: 2.607; 95%CI: 2.077–3.271), and pneumothorax ($P < 0.001$; OR: 1.63; 95%CI: 1.306–2.034), as shown in Table 5.

When studying both factors, ROC curve shows statistically significant results (Table 4 and Fig. 8), with area under the

Table 1: Maternal and neonatal characteristics among the studied group

	Total number [987 (100%)] [*n* (%)]	Survive [573 (58.1%)] [*n* (%)]	Died [414 (41.9%)] [*n* (%)]	*P*
Gestation				
Multiple	102 (10.3)	49 (48)	53 (52)	0.034
Single	885 (89.7)	524 (59.2)	361 (40.8)	
Sex				
Female	429 (42.1)	246 (59.1)	170 (40.9)	0.511
Male	516 (55.6)	313 (57.0)	236 (43.0)	
Missed	22 (2.2)			
Mode of delivery				
Caesarian	566 (57.3)	364 (64.3)	202 (35.7)	<0.001
Vaginal	323 (32.7)	150 (46.4)	173 (53.6)	
Missed	98 (9.9)			
PROM				
No	811 (82.2)	476 (58.7)	335 (41.3)	0.400
Yes	176 (17.8)	97 (55.1)	79 (44.9)	
Sepsis				
No	511 (51.8)	412 (80.6)	99 (19.4)	<0.001
Yes	476 (48.2)	161 (33.8)	315 (66.2)	
Mechanical ventilation				
No	559 (56.6)	516 (92.3)	43 (7.7)	<0.001
Yes	428 (43.4)	57 (13.3)	371 (86.7)	
Pneumothorax				
No	839 (85)	564 (67.2)	275 (32.8)	<0.001
Yes	148 (15)	9 (6.1)	139 (93.9)	
CNS problems				
No	865 (87.6)	557 (64.4)	308 (35.6)	<0.001
Yes	122 (12.4)	16 (13.1)	106 (86.9)	
Hemorrhage				
No	831 (84.2)	560 (67.4)	271 (32.6)	<0.001
Yes	156 (15.8)	13 (8.3)	143 (91.7)	

CNS, central nervous system; PROM, premature rupture of membranes.

Table 2: Hospital stay, Apgar score, weight, and gestational age among the studied group

	Range	Survive		Died		*P*
		Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Days in NICU	2-97	14.6 (13.6)	9 (6-18)	10.3 (10.6)	6 (4-11)	<0.001
Apgar at 5 min	0-9	7.5 (1)	8 (7-8)	7 (1.5)	7 (7-8)	<0.001
Weight (kg)	0.7-5.2	2.5 (0.7)	2.50 (2.0-2.9)	1.8 (0.7)	1.6 (1.3-2.2)	<0.001
GA	26-42	36.0 (2.3)	36 (35 -38)	33 (3.3)	33 (30-35)	<0.001

GA, gestational age; IQR, interquartile range; NICU, neonatal intensive care unit.

curve of 0.588 (95%CI: 0.55–0.625; $P < 0.001$). The factors that showed statistically significant predictors of mortality are Apgar score at 5 min ($P < 0.001$; OR: 0.788; 95%CI: 0.717–0.866), GA ($P < 0.001$; OR: 0.853; 95% CI: 0.791–0.921), sepsis ($P = 0.002$; OR: 1.722; 95% CI: 1.218–2.434), and hemorrhage ($P < 0.001$; OR: 2.202; 95% CI: 1.629–2.978) (Table 5). Odds ratio showed that hemorrhage, sepsis, and pneumothorax have the most effect on mortality, whereas high GA and high Apgar score at 5 min are significant to survival.

Discussion

This study shows that there was a statistically significant association of more deaths with multiple pregnancy, but findings from bivariate analysis and by Cox regression analysis of factors studied before NICU admission showed no statistical significant difference concerning multiple pregnancy. This result is consistent with a systemic review done by Medlock *et al.*, who found that multiple gestation showed an inconsistent effect. It was included in the final model in 8/20 studies, but showed a protective effect for singleton infants in 6 studies and multiple infants in two studies [10]. For example, Yismaw *et al.*[11] found that having singleton pregnancy was 2.18 times higher risk for death of preterm neonates as compared with multiple pregnancies (OR: 2.18; 95%CI: 1.47–3.25). This was in contrary to the findings conducted in Jimma Zone, in northern Ethiopia

and in Ethiopia, DHS data[12] and Haghighi *et al*. [13], who showed that singletons had better survival compared with multiple pregnancies. In other studies, multiple pregnancy was a strong predictor of neonatal death compared with singletons, as reported by Houweling *et al*.[9] (OR: 7.67; 95%CI: 6.43–9.16) and Yeo *et al*.[14] (OR: 1.20; 95%CI: 1.08–1.34). This is in accordance with Bader *et al*. [15], who found that one of the major factors associated with death was multiple births. Lee *et al*.[16] found that in multivariate analyses of data for infants who received intensive care, singleton birth was associated with a reduction in the risk of death before discharge similar to that for a 1-week increase in GA, whereas Shah *et al*.[17] showed that multiple births have no detectable effect on the adjusted composite neonatal outcome of mortality and morbidities.

This study shows that there were more deaths with being male, but this was not statistically significant, and findings from bivariate analysis confirm this result. This is in agreement with Haghighi *et al*.[13], Sankaran *et al*.[18] and Jones *et al*. [19], who could not find a significant difference between

Table 3: Relation between maternal and neonatal characteristics and survival time among studied group

	Mean survival time (95%CI)	Median (95%CI)	*P*
Multiple	25.8 (20.0-31.6)	15.0 (6.6-23.4)	0.210
Single	35.7 (31.2-40.3)	21.0 (16.2-25.8)	
Female	31.8 (27.8-35.8)	23.0 (16.4-29.6)	0.226
Male	34.4 (28.9-39.9)	19.0 (13.5-24.6)	
Caesarian	39.8 (33.6-47.1)	29 (21.125-36.875)	<0.001
Vaginal	27.1 (22-32)	13 (9.957-16.043)	
Mechanical ventilation (N)	82.1 (76.4-87.9)	-	<0.001
Mechanical ventilation (Y)	15.7 (13.6-17.7)	8 (7.1-9.0)	
Sepsis (N)	35.3 (32.7-38)	-	<0.001
Sepsis (Y)	28.3 (24.5-32.1)	13 (10.3-15.7)	
Pneumothorax (N)	49.7 (34.3-55.1)	30 (17.9-42.2)	<0.001
Pneumothorax (Y)	16.2 (13.5-18.9)	10 (8.5-11.5)	
CNS problems (N)	41.1 (36.7-45.6)	30 (23.8-36.2)	<0.001
CNS problems (Y)	20.5 (16.1-24.8)	11 (8.1-14)	
Hemorrhage (N)	44.5 (38.8-50.2)	31 (25.9-36.1)	<0.001
Hemorrhage (Y)	11.7 (9.3-14)	7 (6-8)	
PROM (N)	35.8 (30.9-40.8)	21 (16-26)	0.919
PROM (Y)	31.6 (26-37.3)	23 (13.3-32.8)	

CI, confidence interval; CNS, central nervous system; PROM, premature rupture of membranes; N, no; Y, yes.

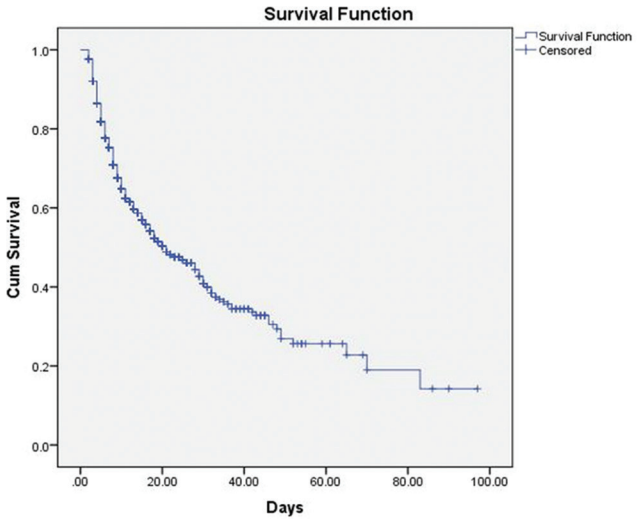

Figure 1: Total neonatal survival curve in relation to time.

Table 4: Predictors for mortality among studied group

	Factors	*P*	Odd ratio	95.0%CI for odd ratio	
				Lower	Upper
Factors before NICU admission	Multiple pregnancy	0.274	0.864	0.664	1.123
	Mode of delivery	0.051	0.749	0.561	1.001
	Weight	0.945	0.989	0.732	1.338
	GA	<0.001	0.816	0.759	0.878
	Apgar score at 5 min	<0.001	0.770	0.703	0.845
Factors after NICU admission	Sepsis	<0.001	1.596	1.243	2.050
	CNS problems	0.651	1.058	0.829	1.349
	Hemorrhage	<.0001	2.607	2.077	3.271
	Pneumothorax	<0.001	1.630	1.306	2.034
Both factors	Multiple pregnancy	0.270	1.248	0.842	1.849
	Mode of delivery	0.508	1.104	0.824	1.480
	Apgar score at 5 min	<0.001	0.788	0.717	0.866
	Weight	0.495	0.894	0.649	1.233
	GA	<0.001	0.853	0.791	0.921
	Sepsis	0.002	1.722	1.218	2.434
	Pneumothorax	0.069	1.301	0.980	1.726
	CNS problems	0.211	1.234	0.888	1.715
	Hemorrhage	<0.001	2.202	1.629	2.978

CI, confidence interval; CNS, central nervous system; GA, gestational age; NICU, neonatal intensive care unit.

Table 5: Results of recessive operator characteristic curve analysis for predicted mortality probabilities calculated in Cox regression analysis

	Area under the curve	*P*	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
Factors before NICU admission	0.547	0.059	0.498	0.595
Factors after NICU admission	0.682	<0.001	0.637	0.728
Both factors	0.588	<0.001	0.550	0.626

NICU, neonatal intensive care unit.

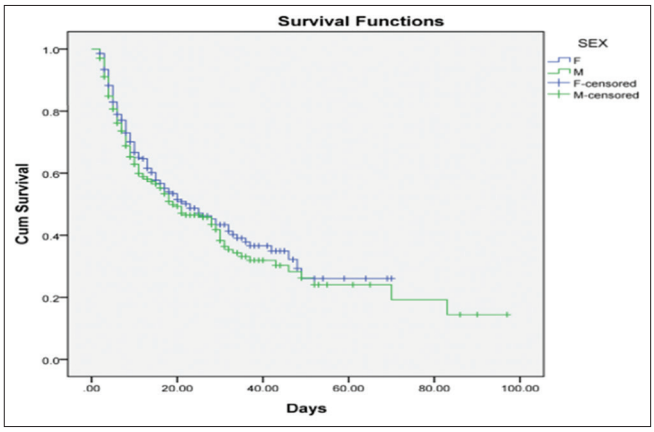

Figure 2: Survival estimation of neonates according to sex in relation to time.

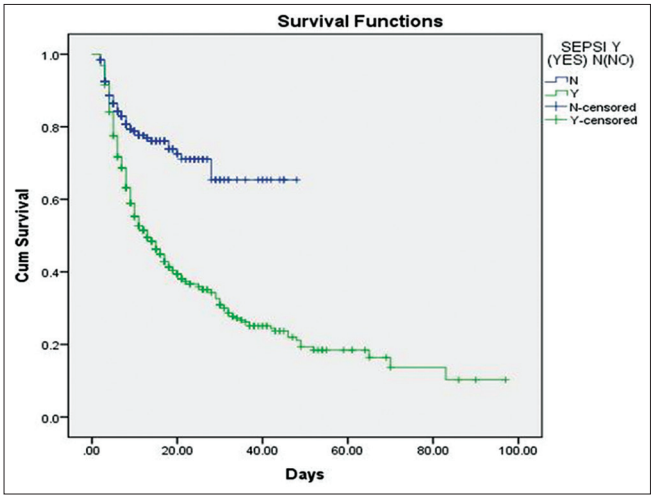

Figure 4: Survival estimation of neonates according to sepsis in relation to time.

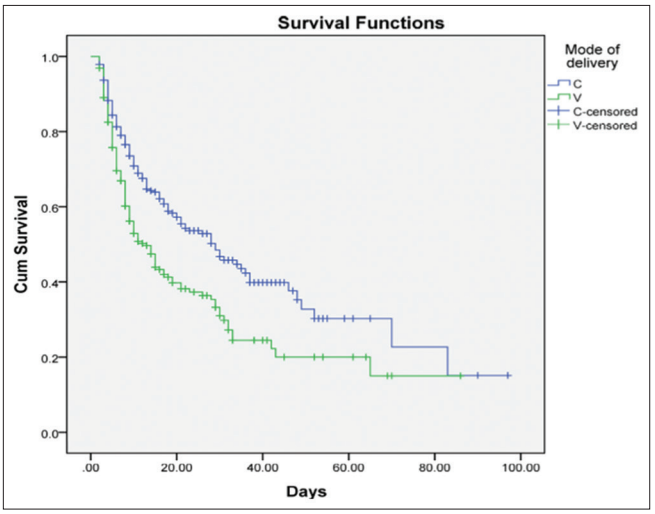

Figure 3: Survival estimation of neonates according to mode of delivery in relation to time.

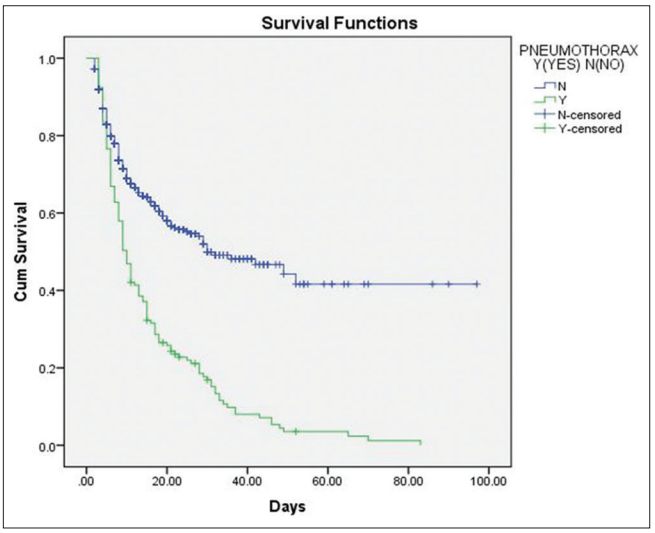

Figure 5: Survival estimation of neonates according to pneumothorax occurrence in relation to time.

male and female sex regarding mortality. On the contrary, Ezz-Eldin *et al*.[4] found that male to female cases were 1.1:1 respectively, with higher mortality in males, and consistent with Zeitlin *et al*. [20], who found that premature births are outnumbered by males with higher susceptibility of mortality. Kolola *et al*.[21] found that being male was a risk factor for neonatal mortality (AOR: 1.85; 95%CI: 1.06–3.26). Saini *et al*.[22] showed a male preponderance (54.3%) regarding neonatal mortality, which is consistent with local literature reported by National Neonatology Perinatal Database (NNPD) in India[23] (52.9% male vs 47% female) and the study by Rakholia *et al*.[24] (63.25% male vs 36.75% female), as well as international studies from Nigeria[25] (54.3% male vs 45.7% female) and from Pakistan[26] (63.75% male vs 36.25% female). In a systemic review done by Medlock *et al*. [10], it was found that female sex (18/30 studies) was frequently found to predict improved survival in multivariate models. Lee *et al*.[17] found in multivariate analyses of data

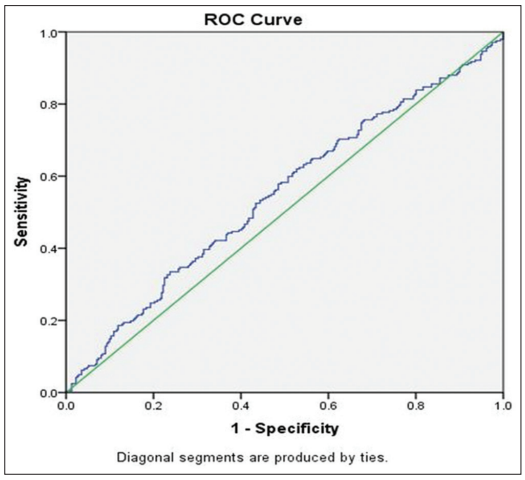

Figure 6: Recessive operator characteristic curve for prediction of neonatal mortality by factors studied before neonatal intensive care unit Admission.

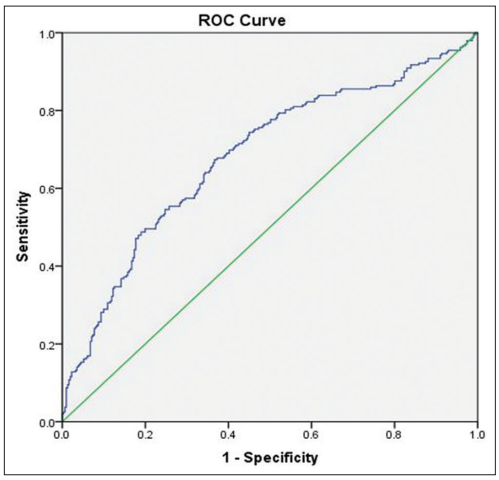

Figure 7: Recessive operator characteristic curve for prediction of neonatal mortality by factors studied after neonatal intensive care unit admission. During the treatment course.

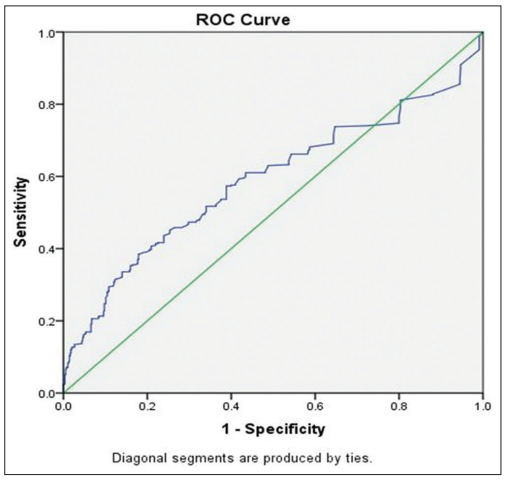

Figure 8: Recessive operator characteristic curve for prediction of neonatal mortality by both factors.

for infants who received intensive care that female sex was associated with a reduction in the risk of death before discharge similar to that for a 1-week increase in GA. Glass *et al*.[27] found that infant girls, on average, have better outcomes than infant boys. Locatelli *et al*.[28] showed that female sex was an independent predictor of survival.

The study results show a statistically significant difference with more deaths with vaginal delivery, and findings from bivariate analysis confirmed. This result, however, by Cox regression analysis was not statistically significant. Our result was consistent with a systemic review done by Medlock *et al*.[10] showing that mode of delivery did not remain significant in the final models (2/25 studies). Malloy found that cesarean section does seem to provide advantages for survival in most immature infants delivered at 22–25 weeks of gestation [29]. However, Haghighi *et al*.[13] evaluated the effect of root of delivery on survival of preterm infants between 22 and 31 weeks and showed 52.8% and 47.3% mortality rate for cesarean and vaginal deliveries, respectively.

Low GA was found to be statistically significant, with more deaths in the present study, which was confirmed by Cox regression analysis, revealing that high GA was statistically significant to survival, with odds ratio of 0.816 (95%CI: 0.759–0.878) when studying factors before NICU admission and 0.853 (95%CI: 0.791–0.921) when studying factors prior and after NICU admission, in agreement with all other studies. Yismaw *et al*.[11] show that as the GA increases by a week, the risk of death was decreased by 18% (AHR of 0.82; 95%CI: 0.74–0.91), which is in line with a study conducted in Jimma University specialized hospital and in Addis Ababa St Paul's Hospital Millennium Medical College [12]. Haghighi *et al*.[13] show that mortality rate increases with decreasing GA. Late preterm has previously shown to be associated with increased risk of hospital death compared with delivery at higher GAs [30]. Abdel Razeq *et al*.[31] found that the neonatal mortality rate was 30 times higher among preterm neonates than among full-term neonates. Prematurity alone was the direct cause of almost 50% of neonatal deaths. Houweling *et al*.[9] found that at the start of delivery, prematurity was a very strong predictor of neonatal death (OR: 11.11; 95%CI: 9.89–12.47). Bader *et al*.[15] found that one of the major factors associated with death was GA. Basu *et al*.[32] found that univariate analysis showed that GA is the factor directly responsible for neonatal mortality. Arafa *et al*.[33] in a multivariate analysis revealed that GA was one of the most important predictors of mortality. This was supported by the clinical evidence that as GA increases, fetal maturity increases and risk of developing different life-threatening complications associated with prematurity may decrease and risk of death reduces [12].

The study shows a statistically significant difference with more deaths with low birth weight; however, by Cox regression analysis, low birth weight was not statistically significant. This was in agreement with a study from NICU in a general

hospital in Porto Algere, Southern Brazil, that included 494 admitted newborns; birth weight has been used, for many years, as a mortality risk indicator for newborn neonates. The birth weight was found to be the indicator that is least able to predict neonatal mortality [34]. However, this was in contrary to most of the other studies, such as Sivasubramaniam *et al*.[35] and Mengesha *et al*. [36], who found that the highest mortality in the NICU was among low-birth-weight admissions. Kolola *et al*.[21] and Malik *et al*.[37] showed that the relative risk of dying owing to low birth weight was 2.66 (95%CI: 1.33–5.33) and 2.68 (95%CI: 2.24–3.2), respectively. Abolfotouh *et al*.[38] found that after adjusting for possible confounders, birth weight ($P = 0.001$) was a significant predictor of survival. Chen *et al*.[39] found that with multiple logistic regression analysis, low birth weight was a significant predictor of unfavorable outcome. Ezz-Eldin and colleagues in Egypt and Grandi and colleagues in Iran found that the lower the birth weight the higher the mortality ($P < 0.001$ and 0.02, respectively) [4,40]. Glass *et al*.[27] found that the extremely low-birth-weight infants (<1000 g) remain at a high risk for death and disability. Locatelli *et al*.[28] showed that birth weight was an independent predictor of survival.

The present study shows that 53% of deaths were in the first week (excluding deaths in first 24 h) and 25% of deaths were in the second week, which was closely related to most of the other studies. Yismaw *et al.*[11] found that 85.23% were within the first 7 days, known as early neonatal death. The study by Sankaran *et al*.[18] revealed that 50% of deaths within 3 days and 75% within 12 days of NICU admission. Abolfotouh *et al*.[38] found that 61% of deaths occurred within the first 3 days, whereas only 3.2% died after the first month. Malik *et al*.[37] found that the incidence of early neonatal death was 82.16%. This finding was in line with the findings reported by Mengesha *et al*. [36], UNICEF [41], a study conducted in Butajira, Ethiopia [42], and a study done by Udo *et al.* [43], revealing that most of the deaths occurred within first 7 days of life. National Neonatal Perinatal Database[44] report in Nigeria stated 82% of mortality in the first 2 days. Ezz-Eldin *et al*.[4] found that the highest mortality rate was in the first few days. This was in consistent with the results reveled form another study based on information from the National Inpatient Sample Database from 1997 to 2004 that included 115 350 very LBW Egyptian infants, which reported that about 50% of death during birth hospitalization occurred in the first three days after delivery [45]. The possible reasons may be attributed to the poor quality of antenatal care, delay in identification, and poor management of complications during pregnancy and birth by health workers.

Low Apgar score and CNS problems were found by the study to be statistically significantly associated with more deaths. Bivariate analysis showed the same results; however, by Cox regression analysis, CNS problems were not statistically significant, but high Apgar score was statistically significant to survival, with odd ratio of 0.770 (95%CI: 0.7–03–0.845) when studying factors before NICU admission and 0.788 (95%CI: 0.717–0.866) when studying factors prior and after NICU admission. This is in agreement with most studies. Mengesha *et al*.[36] found that Apgar score less than 7 and birth asphyxia were the independent predictors for neonatal mortality Sankaran *et al*.[18] found that birth asphyxia was significantly associated with NICU deaths. Locatelli *et al*.[28] in Italy, Abolfotouh *et al*.[38] in Saudi Arabia, and Ogawa *et al*.[46] in Japan found that Apgar score was significant predictor of survival. The study by Malik *et al*.[37] revealed that about 43.94% of babies were admitted with birth asphyxia, which was one of the major causes of mortality, and 50.32% of them developed convulsion. Different institution-based studies have reported the incidence of birth asphyxia ranging from 12.7 to 38.7% [47,48]. In a systemic review done by Medlock *et al*. [10], it was found that higher Apgar score (18/26 studies) was frequently found to predict improved survival, and seizures (3/6 studies) predicted mortality in multivariate models. Basu *et al*.[32] found that the mean Apgar scores at one and five minutes were significantly lower and hypoxic ischemic encephalopathy was more in the dead group. Arafa *et al*.[33] using multivariate analysis revealed that Apgar score less than 7 at 5 min was one of the most important predictor of mortality.

The study results revealed that sepsis was statistically significant with more deaths, and this was confirmed by both bivariate analysis and Cox regression analysis, with odd ratio 1.59 (95%CI: 1.243–2.050) when studying factors after NICU Admission and 1.72 (95%CI: 1.218–2.434) when studying factors prior and after NICU admission. This was in agreement with all other studies, as sepsis was the leading cause of death in studies done by Manzar *et al*.[49] in Pakistan and Ugwu[25] in Nigeria. Sankaran *et al*.[18] and Basu *et al*.[32] found that infection was significantly associated with NICU deaths. Malik *et al*.[37] found that neonatal sepsis was the cause of morbidity in 45.1% of admitted neonates. Different institution-based studies have found the incidence of neonatal sepsis ranging from 17.7 to 70% [50–53]. Gezer *et al*.[54] found that sepsis and infectious complications are the main causes of neonatal morbidity and mortality in preterm deliveries. Alvesa *et al*.[55] found that from 2000 to 2013, there were 745 neonatal deaths, of which 229 (30.7%) had a medical diagnosis of sepsis registered during their course of treatment.

This study finds that there was statistically significant difference with more deaths with PROM, but findings from bivariate analysis showed that there was no statistical significant difference. Gezer *et al*.[54] found that the neonatal mortality rate was 17.5% in PROM cases. Sepsis and infectious complications increase in the presence of PROM. Sepsis and infectious complications are the main causes of neonatal morbidity and mortality in preterm deliveries. Neonatal morbidity and mortality rates increase as the latent period after rupture of membranes lengthens. Toukam *et al*.[56] found that prevalence of PROM for live births was 1.08%, and the overall survival rate was 59.8% at (22-27+6d) weeks of gestation.

The study results reveal that there was a statistically significant difference with more deaths with pneumothorax, and this was confirmed by both bivariate analysis and cox regression analysis, with odd ratio 1.63 (95%CI: 1.306–2.034) when studying factors after NICU admission and 1.3 (95%CI: 0.980–1.726) when studying factors prior and after NICU admission. The studies confirm the high rate of mortality with pneumothorax, such as Navaei *et al.* [57], who found that pneumothorax occurred in 5.8% neonates (mean GA 31 weeks) with 65% mortality. Al Matary *et al*.[58] found that the incidence of pneumothorax was 3.9% with 29.1% mortality, and 21.2% neonates had mechanical ventilation as a predisposing factor of pneumothorax. Approximately 8.7–14% of ventilated neonates experienced at least one episode of pneumothorax. In other studies, the mortality rate varied from 20 to 38% [59]. Therefore, Judicious ventilator strategies, proper sedation, appropriate extubation, readily available X-ray, and surgical facilities help to control this complication.

Hemorrhage, in this study, was statistically significant associated with more deaths, and this was confirmed by both bivariate analysis and Cox regression analysis, with odd ratio of 2.607 (95%CI: 2.077–3.271) when studying factors after NICU admission and 2.2 (95%CI: 1.629–2.978) when studying factors prior and after NICU admission. Iqbal *et al*.[60] found that pulmonary hemorrhage is a life-threatening event in neonates, and prognosis was dismal in patients with this complication. Karthikeyan and Hossain[61] and Anantharaj and Bhat[62] also found a very poor outcome in neonates following pulmonary hemorrhage. Basu *et al*.[32] found that documented intraventricular hemorrhage (IVH) was seen only in expired group of VLBW babies. Chen *et al*.[39] found that with multiple logistic regression analysis, only low-birth-weight and higher IVH grades were the significant predictors of unfavorable outcomes. Therefore, early suspicion, routine screening for IVH, bedside cranial sonography, and adherence to proper preventive measures like sedation probably can lead to better outcome.

The study findings show that mechanical ventilation was statistically significantly associated with more deaths, and findings from bivariate analysis confirmed these results. All the studies confirm the high mortality with mechanical ventilation, such as Iqbal *et al*. [60], who found that mortality in ventilated neonates was 43.3%, which is comparable to mortality of 46% reported by Sangeeta *et al.* [63]. Hossain *et al.*[64] and Mathur *et al.*[65] reported higher figures of 70.6 and 74%, respectively. Singh *et al*.[66] found that mortality in ventilated neonates were 44.5%. Arafa *et al.*[33] with multivariate analysis revealed that mechanical ventilation was one of the most important predictors of mortality.

Study limitations

This study is not free from limitations. First, neonates in our study represent the outcomes of a tertiary perinatal center and are thus not representative of results of other NICUs in Egypt, so a multicenter study is recommended to include different types of hospitals as the outcome of these infants varies from one hospital to another. Second, direct comparison between our figures and those of previous studies may be difficult because of the difference in characteristics of the studied groups. Third, our data were confined to infants admitted to the NICU and hence did not cover deaths of infants who were never admitted to a NICU. Combining data on NICU deaths with data on perinatal deaths occurring without NICU admission should yield information on expected survival at different GAs during pregnancy, which may be helpful to those who counsel pregnant women.

Conclusion

In this study, more than one-third of the neonates died before discharge, and most NICU deaths occurred within the first week after admission. Results show statistically significant difference with more deaths with multiple pregnancy, vaginal delivery, mechanical ventilation, presence of sepsis, pneumothorax, CNS problems, hemorrhage, low GA, low birth weight, low Apgar score at 5 min, and low days of NICU admission, whereas there was no significant statistical difference concerning sex or PROM. Hemorrhage, mechanical ventilation, pneumothorax, CNS problems, vaginal delivery, and sepsis were significant risk factors for time to death, whereas there was no statistical significant difference concerning multiple pregnancy, sex, or PROM. Multivariate analysis showed that hemorrhage, sepsis, and pneumothorax have the most effect on mortality, whereas high GA and high Apgar score at 5 min are significant to survival. This study identified several determinants of neonatal mortality which can serve to design strategies for decreasing neonatal mortality.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Lawn JE, Blencowe H, Oza S, You D, Lee AC, Waiswa P, *et al*. Every newborn: progress, priorities, and potential beyond survival. Lancet 2014;384:189–205.
2. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: when? where? why?. Lancet 2005; 365:891–900.
3. Hamilton BE, Martin JA, Osterman MJK, Curtin SC. Births: preliminary data For 2013. Nat Vital Statistics Rep 2014; 63:1–34.
4. EZZ-Eldin ZM, Abdelhamid TA, Youssef MRL, Nabil H. Clinical Risk Index for Babies (CRIB II) Scoring System in prediction of mortality in premature babies. J Clin Diagn Res 2015; 9:8–11.

5. Lui K, Bajuk B, Foster K, Gaston A, Kent A, Sinn J, *et al*. Perinatal care at the borderlines of viability: a consensus statement based on a NSW and ACT consensus workshop. Med J 2006; 185:495–500.
6. Schuit E, Hukkelhoven CW, Manktelow BN, Papatsonis DN, de Kleine MJ, Draper ES, *et al*. Prognostic models for stillbirth and neonatal death in very preterm birth: a validation study. Pediatrics 2012; 129:e120–27.
7. Stevens SM, Richardson DK, Gray JE, Goldmann DA, McCormick MC. Estimating neonatal mortality risk: an analysis of clinicians' judgments. Pediatrics 1994; 93:945–950.
8. Dorling JS, Field DJ, Manktelow B. Neonatal disease severity scoring systems. Arch Dis Child Fetal Neonatal Ed 2005; 90:F11–F16.
9. Houweling TA, Van Klaveren D, Das S, Azad K, Tripathy PP, Manandhar D, *et al*. A prediction model for neonatal mortality in low- and middle-income countries: an analysis of data from population surveillance sites in India, Nepal and Bangladesh. Int J Epidemiol 2018; 3:1–13.
10. Medlock S, Ravelli ACJ, Tamminga P, MolB WM, Abu-Hanna A. Prediction of mortality in very premature infants: a systematic review of prediction models. PLoS One 2011; 6:e23441.
11. Yismaw AE, Gelagay AA, Sisay MM. Survival and predictors among preterm neonates admitted at University of Gondar comprehensive specialized hospital neonatal intensive care unit, Northwest Ethiopia. Ital J Pediatr 2019; 45:4.
12. Central Statistical Agency (CSA) [Ethiopia] and ICF. *Ethiopia Demographic and Health Survey 2016*. Addis Ababa, Ethiopia, and Rockville, Maryland: CSA and ICF; 2016.
13. Haghighi L, Nojomf M, Mohahbatian B, Najmi Z. Survival predictors of preterm neonates: Hospital based study in Iran (2010-2011). Iran J Reprod Med 2013; 11:957–964.
14. Yeo KT, Lee QY, Quek WS, Wang YA, Bolisetty S, Lui K. Trends in morbidity and mortality of extremely preterm multiple gestation newborns, for the Australian and New Zealand Neonatal Network. Pediatrics 2015; 136: 263–71.
15. Bader D, Kugelman A, Boyko V, Levitzki O, Lerner-Geva L, Riskin A, *et al*. in collaboration with the Israel Neonatal Network. Risk factors and estimation tool for death among extremely premature infants: a national study. Pediatrics 2010; 125: 696–703.
16. Lee HC, Green C, Hintz SR, Tyson JE, Parikh NA, Langer J, *et al*. Prediction of death for extremely premature infants in a population-based cohort. Pediatrics 2010; 126: 644–50.
17. Shah V, Alwassia H, Shah K, Yoon W, Shah P. Neonatal outcomes among multiple births≤32 weeks gestational age; does mode of conception have an impact? A cohort study. BMC Pediatr 2011; 11:54.
18. Sankaran K, Chien LY, Walker R, Seshia M, Ohlsson A. Canadian Neonatal Network. Variations in mortality rates among Canadian neonatal intensive care units. JAMC 2002; 166:173–178.
19. Jones H, Ohlsson A, Peliowski A, Baboolal R, Synnes A, Lee SK, and the Canadian Neonatal Network. Actuarial survival in a large Canadian cohort of preterm and very low birth weight infants. Pediatr Res 1999; 45:246A.
20. Zeitlin J, Saurel-Cubizolles MJ, De Mouzon J, Rivera L, Ancel PY, Blondel B, *et al*. Fetal sex and preterm birth: are males at greater risk?. Hum Reprod 2002; 17:2762–2768.
21. Kolola T, Ekubay M, Tesfa E, Morka W. Determinants of neonatal mortality in North Shoa Zone, Amhara Regional State, Ethiopia. PLoS One 2016; 11:e0164472.
22. Saini N, Chhabra S, Chhabra S, Garg L, Garg N. Pattern of neonatal morbidity and mortality: a prospective study in a District Hospital in Urban India. J Clin Neonatol 2016; 5.
23. National Neonatology Form of India. *National Neonatology Perinatal Database Report for Year 2002-2003*. New Delhi: National Neonatology Form of India; 2003.
24. Rakholia R, Rawat V, Bano M, Singh G. Neonatal morbidity and mortality of sick newborns admitted in a teaching hospital of Uttarakhand. Chrismed J Health Res 2014; 1:228–234.
25. Ugwu GI. Pattern of morbidity and mortality in the newborn special care unit in a tertiary institution in the Niger Delta region of Nigeria: a two year prospective study. Glob Adv Res J Med Med Sci 2012; 1:133–138.
26. Hussain S. Neonatal morbidity and mortality pattern in a tertiary care neonatal unit of a teaching hospital. Ann Pak Inst Med Sci 2014; 10:7–11.
27. Glass HC, Costarino AT, Stayer SA, Brett CM, Cladis F, Davis PJ. Outcomes for extremely premature infants. Anesth Analg 2015; 120:1337–1351.
28. Locatelli A, Roncaglia N, Andreotti C, Doria V, Doni D, Pezzullo JC, *et al*. Factors affecting survival in infants weighing 750 g or less. Eur J Obstet Gynecol Reprod Biol 2005; 123:52–55.
29. Malloy MH. Impact of cesarean section on neonatal mortality rates among very preterm infants in the United States, 2000-2003. Pediatrics 2008; 122:285–292.
30. Swenson AW, Dechert RE, Schumacher RE, Attar MA. The effect of late preterm birth on mortality of infants with major congenital heart defects. J Perinatol 2012; 32:51–54.
31. Abdel Razeq NM, Khader YS, Batieha AM. The incidence, risk factors, and mortality of preterm neonates: a prospective study from Jordan (2012-2013). Obstet Gynecol 2017; 14:28–36.
32. Basu S, Rathore P, Bhatia BD. Predictors of mortality in very low birth weight neonates in India. Singapore Med J 2008; 49:556–560.
33. Arafa MA, Alshehri MA. Predictors of neonatal mortality in the intensive care unit in Abha. Saudi Arabia Med J 2003; 24:1374–1376.
34. Mariani SZ, Renato SP. Comparison between different mortality risk scores in a neonatal intensive care unit. REV Saude Publica 2003; 37:597–602.
35. Sivasubramaniam P, Quinn C, Blevins M, Al Hajajra A, Khuri-Bulos N, Faouri S, *et al*. Neonatal outcomes of infants admitted to a large government hospital in Amman, Jordan. Glob J Health 2015; 7:217–234.
36. Mengesha HG, Wuneh AD, Lerebo WT, Tekle TH. Survival of neonates and predictors of their mortality in Tigray region, Northern Ethiopia: prospective cohort study. BMC Pregnancy Childbirth 2016; 16:202.
37. Malik S, Gohiya P, Khan IA. Morbidity profile and mortality of neonates admitted in Neonatal Intensive Care Unit of a Central India Teaching Institute: a prospective observational study. J Clin Neonatol 2016; 5:168–173.
38. Abolfotouh MA, Al Saif S, Altwaijri WA, Al Rowaily MA. Prospective study of early and late outcomes of extremely low birth weight in Central Saudi Arabia. BMC Pediatr 2018; 18:280.
39. Chen PC, Wang PW, Fang LJ. Prognostic predictors of neurodevelopmental outcome or mortality in very-low-birth-weight infants. Acta Paediatr Taiwan 2005; 46:196–200.
40. Kadivar M, Sagheb S, Bavafa1 F, Moghadam L, Eshrati B. Neonatal mortality risk assessment in a Neonatal Intensive Care Unit (NICU). Iran J Ped 2007; 17:325–331.
41. Wardlaw T, You D, Hug L, Amouzou A, Newby H. UNICEF report: enormous progress in child survival but greater focus on newborns urgently needed. Reprod Health 2014; 11:82.
42. Gizaw M, Molla M, Mekonnen W. Trends and risk factors for neonatal mortality in Butajira District, South Central Ethiopia,(1987–2008): a prospective cohort study. BMC Pregnancy Childbirth 2014; 14:64.
43. National Neonatology Foum India. *Report for Year 2000*. National NeonataologyFoum India; 2000.
44. Udo JJ, Anah MU, Ochigbo SO, Etuk IS, Ekanem AD. Neonatal morbidity and mortality in Calabar, Nigeria: a hospital-based study. Niger J Clin Pract 2008; 11:285–289.
45. Mohamed MA, Nada A, Aly H. Day-by-day postnatal survival in very low birth weight infants. Paediatrics 2010; 126:e360–e366.
46. Ogawa M, Matsuda Y, Kanda E, Konno J, Mitani M, Makino Y, *et al*. Survival rate of extremely low birth weight infants and its risk factors: case-control study in Japan. ISRN Obstetr Gynecol 2013; 2013:873563.
47. Mallick AK, Sarkar UK. One year experience of neonatal mortality and morbidity in a state level neonatal intensive care unit and its comparison with national neonatal-perinatal database. J Indian Med Assoc 2010; 108:738–739.
48. Islam MN, Siddika M, Hossain MA, Bhuiyan MK, Ali MA. Morbidity pattern and mortality of neonates admitted in a tertiary level teaching hospital in Bangladesh. Mymensingh Med J 2010; 19:159–162.
49. Manzar N, Manzar B, Yaqoob A, Ahmed M, Kumar J. The study of etiological and demographic characteristics of neonatal mortality and morbidity – a consecutive case series study from Pakistan. BMC Pediatr

2012; 12:131.
50. Omoigberale AI, Sadoh WE, Nwaneri DU. A 4 year review of neonatal outcome at the University of Benin Teaching Hospital, Benin City. Niger J Clin Pract 2010; 13:321–325.
51. Okechukwu AA, Achonwa A. Morbidity and mortality patterns of admissions into the Special Care Baby Unit of University of Abuja Teaching Hospital, Gwagwalada, Nigeria. Niger J Clin Pract 2009; 12:389–394.
52. Mukhtar-Yola M, Iliyasu Z. A review of neonatal morbidity and mortality in Aminu Kano Teaching Hospital, Northern Nigeria. Trop Doct 2007; 37:130–132.
53. Rajindrajith S, Mettananda S, Adihetti D, Goonawardana R, Devanarayana NM. Neonatal mortality in Sri Lanka: timing, causes and distribution. J Matern Fetal Neonatal Med 2009; 22:791–796.
54. Gezer A, Parafit-Yalciner E, Guralp O, Yedigoz V, Altinok T, Madazli R. Neonatal morbidity mortality outcomes in preterm premature rupture of membranes. J Obstetr Gynaecol 2013; 33:38–42.
55. Alves JB, Gabani FL, Ferrari RAP, Tacla MTGM, LinckJúnior A. Neonatal sepsis: mortality in a Municipality in southern Brazil, 2000 to 2013. Rev Paul Pediatr 2018; 36:132–140.
56. Toukam ME, Luisin M, Chevreau J, Lanta-Delmas S, Gondry J, Tourneux P. A predictive neonatal mortality score for women with premature rupture of membranes after 22-27 weeks of gestation. J Matern Fetal Neonatal Med 2019; 32:258–264.
57. Navaei F, Aliabadi B, Moghtaderi M, Kelishadi R. Predisposing factors, incidence and mortality of pneumothorax in a neonatal intensive care unit in Isfahan, Iran. Zhongguo Dang Dai ErKeZaZhi 2010; 12:417–420.
58. Al Matary A, Munshi HH, Abozaid S, Qaraqei M, Wani TA, Abu-Shaheen AK. Characteristics of neonatal pneumothorax in Saudi Arabia: three years' experience. Oman Med J 2017; 32:135–139.
59. Esme H, Doğru O, Eren S, Korkmaz M, Solak O. The factors affecting persistent pneumothorax and mortality in neonatal pneumothorax. Turk J Pediatr 2008; 50:242–246.
60. Iqbal Q, Younus MM, Ahmed A, Ahmad I, Iqbal J, Charoo BA, *et al*. Neonatal mechanical ventilation: Indications and outcome. Indian J Crit Care Med 2015; 19:523–527.
61. Karthikeyan G, Hossain MM. Conventional ventilation in neonates: experience from Saudi Arabia. Indian J Pediatr 2002; 69:15–18.
62. Anantharaj A, Bhat BV. Outcome of neonates requiring assisted ventilation. Turk J Pediatr 2011; 53:547–553.
63. Mathur NB, Garg P, Mishra TK. Predictors of fatality in neonates requiring mechanical ventilation. Indian Pediatr 2005;42:645–651
64. Sangeeta ST, Rajesh KC, Anurakti S. Study of early predictors of fatality in mechanically ventilated neonates in NICU. Online J Health Allied Sci 2009; 8:3–9.
65. Hossain MM, Mahfuza S, Abdullah MA, Hassan MN, Sahidullah M. Predictors of mortality in ventilated neonates in intensive care unit. Bangladesh J Child Health. 2009;33:77–82
66. Singh M, Deorari AK, Paul VK, Mittal M, Shanker S, Munshi U, *et al*. Three-year experience with neonatal ventilation from a tertiary care hospital in Delhi. Indian Pediatr 1993; 30:783–789.