Predictors of mortality among neonates admitted to neonatal intensive care unit in pediatric Assiut University Hospital, Egypt

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Abstract: Neonatal period is the most hazardous period of life because of various problems/ diseases which a neonate faces. There is great over lap between the risks associated with morbidity and mortality in the perinatal and neonatal periods. The present study aimed to identify the profile and risk factors for neonatal mortality among neonates admitted to neonatal intensive care unit (NICU) in pediatric Assiut University Hospital (AUH). A prospective study was conducted in NICU of pediatric AUH. Study population included all neonates admitted to NICU over a period of one year. The data collected included detailed antenatal and natal histories, details of clinical examination, primary diagnosis, progress during the hospital stay and outcome. The outcome measure was in-hospital death. Survival was defined as the discharge of a live infant from the NICU. Differences between deceased and survived neonates were estimated by the chi-square test and t-test. The association between risk factors and neonatal mortality were estimated by relative risk. The significance level used was p-value of less than 0.05. A total of 990 neonates were included in the study, of which 582 neonates (58.8%) died during their hospital stay. The mortality rate decreased with the increase in birth weight, as well as gestational age. Respiratory distress was the commonest primary diagnosis (94.5%) among all admitted neonates, followed by very low birth weight (VLBW) (36.7%), congenital malformations (8.2%), and infections (4.4%). Significant risk factors (P<0.05) associated with neonatal mortality were: vaginal delivery, multiple births, low Apgar score at 5 minutes, neonatal respiratory distress, prematurity, and low birth weight (LBW). It is concluded that majority of the causes of neonatal mortality are preventable**.** Surveillance programs for neonatal death should include preventive actions and interventions for the perinatal period. Focused initiatives for quality improvement may also be necessary.
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Key words: mortality, neonates, admission, neonatal intensive care unit.

1. Introduction:

Neonatal death is a serious concern, both in the developing and developed worlds. While infant mortality rates have been decreasing steadily all over the world, changes in neonatal mortality have been much slower [1, 2].

Accurate documentation of fetal and neonatal deaths enables analysis of change in perinatal death rates over time and assessment of their preventability. It is recommended that such audit should occur both regionally and nationally [3].

Neonatal period (0 to 28 days of life) is the most hazardous period of life because of various problems/diseases, which a neonate faces. A large majority of newborn babies do not develop any serious problem or difficulties and require only minimal care, which can be provided by the mother if properly supervised by a health worker. High risk mothers are likely to give birth to preterm or low birth weight babies who suffer a large number of problems[4]. Majority of the causes of neonatal morbidity are preventable[5]. Some of the newborns in developing countries have an impaired growth right during their intrauterine life, reflecting the nutritional status of the mother[6]. About 42% of the infant deaths in our country occur within first 28 days of life[7]. Prematurity accounts for majority of high risk newborns as they face a large number of problems[8].

Neonatal morbidity and mortality is on increase day by day due to lack of the available resources in developing countries. This can be reduced by proper and timely intervention[9].

A considerable share of these deaths results from avoidable causes, which means that interventions could have been effective. However, reducing neonatal mortality is hindered by the complex and close relationship between biological and social factors, and by the coverage and quality of health services during prenatal care, delivery and neonatal period.[10] For better neonatal care and prevention of the preventable causes of neonatal morbidity and mortality, this study was conducted in neonatal intensive care unit (NICU) in pediatric Assiut University Hospital in order to identify the profile and risk factors for neonatal mortality among admitted neonates.

2. Subjects and Methods

A prospective study was conducted in neonatal intensive care unit (NICU) in pediatric Assiut University Hospital (AUH), Assiut city, Egypt. Study population included all neonates admitted to NICU over a period of one year. The outcome measure was in hospital death. Survival was defined as the discharge of a live infant from the hospital.

The indications for admission in NICU in pediatric AUH are preterm birth or premature (<37 weeks of gestation), respiratory distress, infections, congenital malformations, birth asphyxia, multiple births, VLBW (<1500), and others.

Data collected included detailed antenatal and natal histories; gestational age, gender, birth weight, single or multiple births, presence of meconium-stained amniotic fluid and type of delivery (vaginal or caesarian section). In addition, data included maternal variables as parity, history of abortion, obstructed labor, bleeding and antenatal morbidity. Apgar scores at 5 minutes, details of clinical examination, primary diagnosis and progress during the hospital stay, and outcome were recorded. Data were obtained from hospital records and oral communication with the attending physicians, as well.

All data were revised, coded and subjected to computer entry and analysis. Statistical analysis was performed using statistical package for social sciences (SPSS) version 11. Descriptive statistics (frequency and percentage) were used to present distribution of study population. Differences between survived and deceased neonates were estimated by the chi-square test and t-test. The association between risk factors and mortality were estimated by relative risk (RR) and their corresponding 95% confidence interval (CI). The significance level used was P-value of less than 0.05.

3. Results

A total of 990 neonates fulfilled the inclusion criteria of the study; of which a total of 582 (58.8%) babies died during the hospital stay. Most neonatal deaths (n=449, 77.1%) occurred during the first week after admission to NICU. Premature neonates (n = 768) constituted 77.6%, and very low birth weight (n = 363) constituted 36.7% of all neonates admitted to NICU during the period of the study. Mean birth weight of survived neonates was significantly more than that of deceased (2.37kg ± 0.77 versus 1.64kg ± 0.76, p<0.0001). (data not in table).

The mortality rate decreased with the increase in birth weight as well as gestational age. None of the neonates below 27 weeks gestational age survived, and 96.1% of those weighing less than 1000g died (Table 1).

Primary causes of mortality are summarized in table (2). Common causes of mortality in LBW neonates (<2500g) were respiratory distress and prematurity, and both of them decreased as the birth weight increased. Among those with normal birth weight, common causes of mortality were respiratory distress (90.4%), prematurity (27.7%), congenital malformations (26.5%), hypoglycemia (14.5%), infections (8.4%) and brain insult due to hypoxia (8.4%).

Table (3) shows a comparison between premature and full term neonates as regards primary cause of death. Among premature neonates the most important was respiratory distress syndrome (97.9%). Among full term, in addition to respiratory distress (82.9%), other important causes were congential malformations (21.6%), hypoglycemia (10.8%), infections (9.0%) and brain insult (8.6%).

Maternal and fetal variables were compared between the survived and the deceased neonates (Table 4). Risk factors significantly associated with mortality were twin pregnancy (RR 1.36), vaginal delivery (Vs. caesarian) (RR 1.22), and low Apgar score at 5 minutes (RR 1.30).

Table (5) shows relative risk of various morbidities. The risk factors most closely associated with neonatal mortality were respiratory distress (RR 1.92), prematurity (RR 1.84), low birth weight (RR 2.0), and very low birth weight (RR 2.02).

Table (1): Distribution of neonates admitted to NICU by birth weight and gestational age

Birth weight (g)	Gestational age (weeks)														Total	Mortality No. (%)
	25-26		27-28		29-30		31-32		33-34		35-36		≥ 37			
	T	D	T	D	T	D	T	D	T	D	T	D	T	D		
500 -	35	35	46	44	16	14	5	5	0	0	0	0	1	1	103	99 (96.1)
1000 -	3	3	70	62	104	98	48	34	24	12	8	5	3	1	260	215 (82.7)
1500 -	0	0	11	9	46	31	75	39	64	37	13	7	10	4	219	127 (58.0)
2000 -	0	0	0	0	6	5	17	8	46	16	52	16	40	13	161	58 (36.0)
≥ 2500	0	0	2	2	3	0	4	4	12	3	58	14	168	60	247	83 (33.6)
Total	38	38	129	117	175	148	149	90	146	68	131	42	222	79	990	582 (58.8)

T: Total, D: Died

Table (2): Distribution of deceased neonates by birth weight and primary cause of death

Cause of death	Birth wt (g)					
	500- (n=99) No. (%)	1000- (n=215) No. (%)	1500- (n=127) No. (%)	2000 – (n=58) No. (%)	≥ 2500 (n=83) No. (%)	Total (n=582) No. (%)
Respiratory disease	96 (97)	212 (98.6)	126 (99.2)	56 (96.6)	75 (90.4)	565 (97.1)
Prematurity	98 (99)	214 (99.5)	123 (96.9)	45 (77.6)	23 (27.7)	503 (86.4)
Congenital malformations	0 (0.0)	4 (1.9)	6 (4.7)	12 (20.7)	22 (26.5)	44 (7.6)
Infections	2 (2.0)	7 (3.3)	5 (3.9)	1 (1.7)	7 (8.4)	22 (3.8)
Hypoglycemia	0 (0.0)	1 (0.5)	1 (0.8)	1 (1.7)	12 (14.5)	15 (2.6)
Brain insult	0 (0.0)	0 (0.0)	1 (0.8)	2 (3.4)	7 (8.4)	10 (1.7)
Coagulopathies	1 (1.0)	1 (0.5)	1 (0.8)	1 (1.7)	1 (1.2)	5 (0.9)
Birth injuries	0 (0.0)	1 (0.5)	0 (0.0)	1 (1.7)	1 (1.2)	3 (0.5)
Heamolysis and blood diseases	0 (0.0)	0 (0.0)	3 (2.4)	0 (0.0)	2 (2.4)	5 (0.9)

Table (3): Primary diagnosis among preterm and full-term neonates admitted to NICU

Disease	Preterm (n=768) No. (%)	Full term (n=222) No. (%)	Total (n=990) No. (%)	P-value
Respiratory system disease	752 (97.9)	184 (82.9)	936 (94.5)	0.000
Very low birth weight (<1500g)	359 (46.7)	4 (1.8)	363 (36.7)	0.000
Congenital malformations	33 (4.3)	48 (21.6)	81 (8.2)	0.000
Infections	24 (3.1)	20 (9.0)	44 (4.4)	0.000
Endocrinopathies	13 (1.7)	24 (10.8)	37 (3.7)	0.000
Brain insult	6 (0.8)	19 (8.6)	25 (2.5)	0.000
Hypoglycemia	6 (0.8)	6 (2.7)	12 (1.2)	0.030
Birth injuries	3 (0.4)	4 (1.8)	7 (0.7)	0.049
Haemolysis and blood disease	9 (1.2)	13 (5.9)	22 (2.2)	0.000

Table (4): Comparison of maternal and infant variables between survived and died neonates

variable	Survived (n=408) No. (%)	Died (n=582) No. (%)	P-value	Relative risk (95% CI)
Primipara	25 (6.1)	42 (7.2)	0.295	1.07 (0.88 – 1.30)
History of abortion	107 (26.2)	165 (28.4)	0.253	1.04 (0.93 – 1.17)
Maternal Diabetes	12 (2.9)	6 (1.0)	0.025	0.56 (0.29 – 1.08)
Hypertensive disease of pregnancy	63 (15.4)	92 (15.8)	0.475	1.01 (0.88 – 1.17)
Bleeding per vagina	30 (7.4)	51 (8.8)	0.250	1.08 (0.90 – 1.29)
Obstructed labor	14 (3.4)	9 (1.5)	0.043	0.66 (0.40 – 1.10)
Female neonate	142 (34.8)	230 (39.5)	0.075	1.09 (0.98 – 1.21)
Twin pregnancy	79 (19.4)	208 (35.7)	0.000	1.36 (1.23 – 1.51)
Vaginal delivery	160 (39.2)	298 (51.2)	0.000	1.22 (1.10 – 1.35)
Meconium- stained amniotic fluid	20 (4.9)	9 (1.5)	0.002	0.52 (0.30 – 0.89)
Apgar score < 5 at 5 minutes	29 (7.1)	81 (13.9)	0.048	1.30 (0.98 – 1.32)

Table (5): Relative risk of various morbidities among neonates admitted to NICU

Primary diagnosis	Discharged (n=408) No. (%)	Died (n=582) No. (%)	P-value	Relative risk (95% CI)
Low birth weight (<2500 g)	244 (59.8)	499 (85.7)	0.000	2.00 (1.67 – 2.40)
Very low birth weight (<1500 g)	49 (12)	314 (54.0)	0.000	2.02 (1.83 – 2.24)
Respiratory distress	371 (90.9)	565 (97.1)	0.000	1.92 (1.29 – 2.85)
Prematurity	265 (65)	503 (86.4)	0.000	1.84 (1.53 – 2.21)
Congenital malformations	37 (9.1)	44 (7.6)	0.231	0.92 (0.75 – 1.13)
Infection	22 (5.4)	22 (3.8)	0.146	0.85 (0.63 – 1.14)
Hypoglycemia	22 (5.4)	15 (2.6)	0.026	0.68 (0.46 – 1.01)
Brain insult	15 (3.7)	10 (1.7)	0.043	0.68 (0.42 – 1.09)
Coagulopathies	7 (1.7)	5 (0.9)	0.179	0.71 (0.36 – 1.38)
Birth injuries	4 (1.0)	3 (0.5)	0.313	0.73 (0.31 – 1.71)
Haemolysis and blood diseases	17 (4.2)	5 (0.9)	0.001	0.38 (0.18 – 0.83)

4. Discussion:

A considerable variation of mortality rates across NICUs was found. In our study, we documented a very high mortality rate of 58.8%, compared to other studies reporting mortality at NICUs. This may be contributed to higher percentages of preterm and LBW which are the commonest predisposing factors of neonatal mortality. In addition, it is notable that our study was conducted in a university hospital, which serves exclusively the public health sector and is the reference center for high risk pregnancies in the whole governorate. Furthermore, complicated deliveries are usually referred after many failed trials at the primary level with poor equipment and less experienced staff. Other studies have documented a mortality rate varying from 23% to 37% [1,11,12,13,14]. Most of these studies were Indian. A wide variations in the mortality rates was found among NICUs in a Brazilian study (10 – 48%)[10]. A large Canadian study investigated mortality rates for infants admitted to 17 NICUs (n = 19,265), and reported a very low overall mortality rate of 4%. Variations in mortality rates are important, as they would reflect variations in quality of care [15].

Prognosis depends not only on birth weight and gestational age, but also on other perinatal factors and physiological conditions of the individual infants, in particular, disease severity in the first hours of life[1].

Birth weight and 5-min Apgar score were found to be independent predictors of neonatal mortality and had similar accuracy in discriminating the groups of newborns at high risk for death. While Apgar score can be somewhat inaccurate due to subjective evaluation, birth weight provides a more precise measurement for screening neonates at risk of dying. The cutoff value of 2,500g for birth weight achieved the best performance for predicting neonatal death with sensitivity higher than 70%. Birth weight has been widely recognized as a powerful predictor of infant death, alone or in conjunction with other potential risk variables[10,16].

In the present study, the mean birth weight of newborns admitted to the NICU was 1,944g ± 842g. The risk of dying was found to decrease with the increase in birth weight and gestational age. Apgar score was found to be a significant variable in the study. The mean Apgar scores at 5 min were significantly lower in the deceased group.

Results of several studies conducted in developing and developed regions have found gestational age as a powerful predictor of neonatal mortality[15,17]. The present study showed that preterm newborns had higher risk of dying (RR, 1.84) compared to full term newborns.

A national study of perinatal/neonatal mortality confirmed the suspecion that Egypt has transitioned in to a different epidemiological model where immediate complications of delivery and prematurity have become more significant contributors to neonatal mortality than infection. The study documented that prematurity and respiratory distress contributed to 57% of deaths while infection represented only 7% of neonatal deaths [(2)] . This was in agreement with our study.

We found that congenital anomalies caused 7.6% of neonatal deaths in accordance with the national study, but in contrast to others in developed countries. Wong *et al*. [(3)] found that congenital malformations (29.6%) represented the commonest cause of neonatal deaths despite of thorough antenatal and early termination of pregnancy in presence of major congenital malformations. On the other hand respiratory distress caused only 9.6% of neonatal mortality. The same was reported by Sankaran *et al.* [(15)]. These differences in pattern of neonatal mortality may be due to marked advances in the developed countries concerning neonatal mechanical ventilation and management of preterm neonates together with dealing properly with neurological sequels of hypoxia and routine use of surfactant in respiratory distress syndrome. All these factors caused regression of respiratory distress and prematurity as main contributors to neonatal deaths.

A number of antenatal and intrapartum factors have been reported in the literature to be significantly associated with perinatal and neonatal deaths. In the present study, only maternal risk factors found to be significantly associated with mortality of neonates were multiple births and vaginal delivery. Maternal factors found to be significantly associated with neonatal mortality were history of abortion, bleeding per vagina and failure to give steroids antenatally at least 24 hours prior to childbirth[(1,18)].

Forssas *et al.* [(19)] found that among maternal predictors of perinatal mortality are: in-vitro fertilization, previous stillbirth, higher maternal age, maternal diabetes, lower socioeconomic status, smoking during pregnancy, and first birth. They also conclude that excess mortality due to maternal risk factors occurred mainly through their tendency to cause LBW. However, the excess mortality associated with low socioeconomic status and diabetes was mediated by other mechanisms in addition to LBW.

Our study showed that the risk factors most closely associated with neonatal mortality in NICU were respiratory distress (RR, 1.92), prematurity (RR, 1.84), low birth weight (RR, 2.00), and very low birth weight (RR, 2.02). Female gender, multiple births, vaginal delivery, and low Apgar score at 5 minutes also posed neonates at higher risk of mortality.

Locatelli *et al.*[(20)] showed that smaller gestational age and birth weight, female gender, low five-minute Apgar score and failure of steroid administration were independent predictors of survival.

Chen *et al.*[(21)] found that, with multiple logistic regression analysis, only low birth weight and intraventricular haemorrhage grades were the significant predictors of unfavorable outcomes.

Brito *et al.*[(11)] showed that very low birth weight infants with birth weight less than 750g, less than 29 weeks gestational age and CRIB (clinical risk index for babies) scores above ten had higher mortality rate.

Some limitations of the present study should be addressed. Data were restricted to infants admitted to NICU and hence did not cover deaths of those who did not reach any specialized care. Combining data on NICU deaths with data on deaths occurring in other settings should yield information on predictors of neonatal deaths for all infants born in the community, which may be helpful for those counseling pregnant women. In this sense, further studies should assess suitable algorithms useful for screening all neonates. Moreover, there was a lack of refined clinical information on disease severity, a potential confounder. These data are not recorded on a standardized basis in NICU thus they could not be used as a source of data. Therefore, some clinical information on pregnancy and delivery is out of the scope of this study.

In conclusion, most NICU deaths occurred within the first few days after admission. Respiratory distress, low birth weight, prematurity, congenital malformations were the major causes of neonatal admission to NICU in our study. Low birth weight, respiratory distress, and prematurity were the conditions which posed the admitted neonates at higher risk of death.

The strong association between NICU mortality rates on the hand and low birth weight and prematurity on the other indicates the importance of antenatal care, prevention of preterm deliveries and transfer of mothers with high risk pregnancies to tertiary-level perinatal centers before delivery as the uterus is the best incubator for a premature baby.

The results of the present study suggest that surveillance programs for neonatal death should include preventive actions and interventions for the delivery period. Focused initiatives for quality improvement may also be necessary. Development of strategies aimed at addressing these issues is a key to further reduction of NICU deaths.

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