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Original Article

Prognostic factors for neonatal mortality at the Agadir regional hospital centre, Morocco: A cohort study

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الملخص

أهداف البحث: على الرغم من انخفاض معدل وفيات الأطفال حديثي الولادة على مستوى العالم، إلا أن التقدم بطيء للغاية والتأخير ملحوظ بشكل عام في أفريقيا. الهدف من الدراسة هو تحديد العوامل التنبؤية المرتبطة ببقاء الأطفال حديثي الولادة في مركز أكادير الإقليمي للمستشفى، المغرب.

طريقة البحث: أجريت دراسة مجموعة استعادية في قسم حديثي الولادة في مركز أكادير الإقليمي للمستشفى. تم تضمين الأطفال حديثي الولادة الذين تتراوح أعمارهم بين صفر و ٢٨ يوما، والذين تم إدخالهم إلى المستشفى بين ١ يناير و٩ مايو ٢٠٢٢م في هذه الدراسة. تم تحديد عوامل تنبؤية مختلفة في التحليل أحادي المتغير بعد طريقة تحليل بقاء كابلان ماير ومقارنة معدلات البقاء باستخدام اختبار الرتبة اللوغاريتمية. تم استخدام نموذج كوكس لتحديد العوامل المرتبطة ببقاء الأطفال حديثي الولادة.

النتائج: تم تضمين ما مجموعه ٦٣٩ مولودا جديدا، تم إدخال ٩٥،٩٪ منهم إلى المستشفى خلال الأسبوع الأول من حياتهم. توفي ١١٥ مولودا، وهو ما يمثل معدل وفيات حديثي الولادة في المستشفى بنسبة ١٨٪. ومن بين المواليد الذين ماتوا، كانت نسبة ٩٨،٣٪ وفيات مبكرة لحديثي الولادة. وكانت العوامل المرتبطة بزيادة خطر الوفاة هي الاختناق أثناء الولادة والولادة المبكرة وعمر حديثي الولادة أقل من أو يساوي ٧ أيام وانخفاض الوزن عند الولادة وانخفاض حرارة الجسم.

الاستنتاجات: لا يزال معدل وفيات الأطفال حديثي الولادة مرتفعا. إن تطوير مهارات الجهات الفاعلة وتعزيز الفحص للحمل الخطير مع الإنعاش المعزز والرعاية المبكرة للمواليد الجدد أمر ضروري للحد من وفيات الأطفال حديثي الولادة.

الكلمات المفتاحية: في المستشفى؛ وفيات الأطفال حديثي الولادة؛ العوامل التنبؤية؛ البقاء على قيد الحياة؛ المغرب؛ دراسة الأقران

Abstract

Introduction: Although neonatal mortality is declining globally, progress is slow, particularly in Africa. The goal of this study was to determine the predictive factors associated with survival in newborns at the Agadir Regional Hospital Centre, Morocco.

Methods: This retrospective cohort study performed at the neonatology department of the Agadir Regional Hospital Centre included neonates, from birth to 28 days old, who were hospitalized between January 1 and May 9, 2022. Prognostic factors were determined through univariate analysis with the Kaplan–Meier survival analysis method, and survival rates were compared with the log-rank test. The Cox model was used to determine factors associated with neonatal survival.

Results: Of 639 enrolled newborns, 95.9 % were hospitalized during the first week of life. A total of 115 newborns died, resulting in an in-hospital neonatal mortality rate of 18 % (95 % CI [15.2–21.2]), and 98.3 % were

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early neonatal deaths. The factors associated with elevated death risk were perinatal asphyxia ($_{a}$HR = 2.61, 95 % CI [1.57−4.43], p < 0.001); prematurity ($_{a}$HR = 2.15, 95 % CI [1.17−3.94], p = 0.013); neonatal age ≤7 days ($_{a}$HR = 4.89, 95 % CI [1.14−20.94], p = 0.032); low birth weight ($_{a}$HR = 2.25, 95 % CI [1.28−3.94], p = 0.005); and hypothermia ($_{a}$HR = 7.60, 95 % CI [1.71−33.73], p = 0.008).

Conclusion: The neonatal mortality rate remains high. Developing the skills of healthcare providers, strengthening risk screening for pregnancies, and enhancing resuscitation and early care for newborns are essential to decrease neonatal mortality.

Keywords: Cohort study; In-hospital; Morocco; Neonatal mortality; Prognostic factors; Survival analysis

Introduction

The neonatal period, the first 28 days of life, is the most critical period in terms of risk of dying.[1] The first 5 years of life account for 85 % (5.3 million newborns) of all child and adolescent deaths, of which 47 % occur in the neonatal period, approximately 75 % occur in the first 7 days of life, and one-third occur on the day of delivery, thus totaling approximately 7000 newborn deaths every day.[1,2] In 2018, the newborn mortality rate (NMR) was 18 deaths per 1000 live births worldwide and 16 per 1000 live births in North Africa.[1,3] In Morocco, from 2003 to 2018, the NMR decreased from 27 to 13.6 per 1000 live births.[4] Since 1990, the survival of children has substantially increased worldwide. Globally, the number of newborn fatalities decreased to 2.4 million in 2019. Nonetheless, the decrease in newborn death has been less rapid than the decrease in mortality in children under 5 years of age.[2] Between 2019 and 2030, more than 26 million neonatal deaths are expected occur.[5] The most newborn fatalities occur in low- and middle-income nations.[2] Prematurity, perinatal hypoxia, and newborn infections account for 80 % of neonatal deaths.[5,6] Moreover, approximately four cases of "near miss" births occur for each case of neonatal death.[7] "Neonatal near miss" refers to any newborn with a serious complication during the first days of life, who escaped death and survived during the neonatal period.[8] A total of 1.3 million newborns survive with major disability, and 1 million survive with moderate or mild disability. Most of these deaths and disabilities are preventable.[5] In Morocco, the near miss rate is between 2.6 and 10 times greater than the newborn mortality rate.[9] In 2021, 88.5 % [88.3−90.7 %] was the near miss rate reported by the National Reference Centre for Neonatology and Nutrition in Morocco.[10] To increase neonates' chances of survival and health, and eliminate avoidable deaths, the first Sustainable Development Goal is achieving ≤12 deaths per 1000 live births by the year 2030 all countries, as well as continued decreases in deaths and disabilities, thus ensuring that no newborn is overlooked.[5] To achieve this goal, high quality prenatal, birth, and postnatal care coverage for mothers and their newborns, as well as hospital care, will be essential.[2] The goal of this investigation was to identify predictive variables associated with newborn survival at the Regional Hospital of Agadir, Morocco.

Materials and Methods

Study type, setting, and duration

This investigation used a retrospective cohort design and was performed at the neonatal unit of the Hassan II regional hospital in Agadir between January 1 and May 9 of 2022. This level II neonatal intensive care unit reference center in the Souss Massa region has a bedding capacity of 18, ten heating tables, and five self-propelled syringes. The center receives and provides care for newborns with health problems, who are referred from the regional maternity hospital, provincial hospitals, birthing centers, and clinics in the city of Agadir and neighboring southern regions.

Study population and eligibility criteria

This study included all newborns younger than 28 days of age who were hospitalized at the neonatology department during the study period, regardless of the reason for admission. Stillbirths or newborns older than 28 days were excluded from the study.

Study variables

Dependent variable

The dependent variable was neonatal mortality, defined as death of any newborn within the first 28 days of life after birth. In accordance with the WHO definition of neonatal mortality, late neonatal mortality is defined as death occurring after the seventh day of life, and early neonatal mortality is defined as death occurring within the first week of life.[11,12]

Independent variables

The study's independent variables were age (≤7 days: early neonatal period; >7 days: late neonatal period),[11,12] sex, weight (<2500 g: low weight; ≥2500 g: normal weight),[13] referral service, origin, amniotic fluid color abnormalities, perinatal asphyxia, neonatal infection, jaundice, prematurity, hemorrhagic syndrome, multiple pregnancy, malformation, HIV(+) mother, maternal−fetal incompatibility, mother with diabetes, mother with pre-eclampsia, hypothermia (temperature <36.5 °C), mother in intensive care, home delivery, and gastrointestinal disease.

Data collection

A data collection sheet enabled gathering of clinical and sociodemographic information from hospital birth and death registers, as well as clinical records for hospitalized newborns. To prevent selection bias and ensure the quality of data collection, we included all records for hospitalized newborns during the study period. To avoid information bias, standardization of definitions and variables was used.

Additionally, the team members responsible for data extraction received training, and the data collection tool was tested to ensure uniformity and avoid potential errors. After cross-checking of information sources (registers and patient records), the extracted data were also examined, and the team together verified the findings. Finally, to avoid confounding bias, multivariate analysis was performed.

The original date was the date of birth, and the last news date was the day of hospital discharge. Newborns discharged alive were censored at the date of hospital release.

Data management and analysis

The statistical analysis was performed with JAMOVI 21. By subtraction of the date of hospital discharge or death from the date of birth, the length of the risk period for death was computed in days for each newborn. Qualitative variables are presented as numbers and proportions. Newborn survival was estimated with the Kaplan−Meier method, and survival curves from various groups were compared with log-rank tests. The Cox regression model was used to identify factors associated with neonatal survival. Variables significantly associated with survival in the univariate analysis with $p \leq 0.05$ were introduced into the multivariate model. Hazard ratios (HR) with 95 % confidence intervals (95 % CIs) were computed. The significance threshold was 0.05.

Results

Demographic and clinical characteristics

Between January 1 and May 9 of 2022, we collected data for 115 cases of neonatal death among the 639 enrolled newborns, corresponding to an 18.0 % (95 % CI [15.2−21.2]) in-hospital NNM rate, among which 98.3 % of deaths (113/115) were early neonatal mortality cases. Among the included newborns, 95.9 % were hospitalized during their first week of life, and 57.6 % were boys. The average weight of the newborns was 2690 ± 901 g, 39.4 % had low birth

Table 1: Distribution of demographic and clinical characteristics among the 639 newborns hospitalized in the neonatology department of the Regional Hospital Center of Agadir, Morocco.

Variables	Total n (%) (N = 639)	Outcomes, n (%)		p-value
		Survived 524 (82)	Died 115 (18)	
Sex				0.728
Male	368 (57.6)	304 (47.6)	64 (10)	
Female	271 (42.4)	220 (34.4)	51 (8)	
Neonatal age at admission				**0.003**
≤7 days	613 (95.9)	500 (78.2)	113 (17.7)	
>7 days	26 (4.1)	24 (3.8)	2 (0.3)	
Birth weight				**<0.001**
<2500 g	207 (39.4)	149 (28.4)	58 (11)	
≥2500 g	318 (60.6)	286 (54.5)	32 (6.1)	
Reference service				**0.024**
Maternity	254 (39.7)	223 (34.9)	31 (4.9)	
Emergency	385 (60.3)	301 (47.1)	84 (13.1)	
Origin				0.107
Urban	403 (78.1)	327 (63.4)	76 (14.7)	
Rural	113 (21.9)	100 (19.4)	13 (2.5)	
Amniotic fluid color abnormality	29 (4.6)	28 (4.5)	1 (0.2)	**0.055**
Perinatal asphyxia	285 (45.7)	218 (34.9)	67 (10.7)	**0.002**
Neonatal infection	30 (4.8)	27 (4.3)	3 (0.5)	0.160
Jaundice	38 (6.1)	38 (6.1)	0 (0)	**0.003**
Prematurity	221 (35.4)	159 (25.5)	62 (9.9)	**<0.001**
Hypothermia	3 (0.5)	1 (0.2)	2 (0.3)	**<0.001**
Digestive disease	9 (1.4)	7 (1.1)	2 (0.3)	0.96
Hemorrhagic syndrome	207 (39.4)	149 (28.4)	58 (11)	**<0.001**
Malformation	24 (3.8)	19 (3)	5 (0.8)	0.861
HIV(+)* mother	7 (1.1)	7 (1.1)	0 (0)	0.21
Maternal-fetal incompatibility	4 (0.6)	3 (0.5)	1 (0.2)	0.80
Diabetic mother	15 (2.4)	15 (2.4)	0 (0)	0.09
Pre-eclamptic mother	2 (0.3)	2 (0.3)	0 (0)	0.61
Mother in intensive care	5 (0.8)	5 (0.8)	0 (0)	0.39
Home delivery	2 (0.3)	2 (0.3)	0 (0)	0.61

Note: *HIV(+): human immunodeficiency virus (positive). Significant at $p \leq 0.05$.

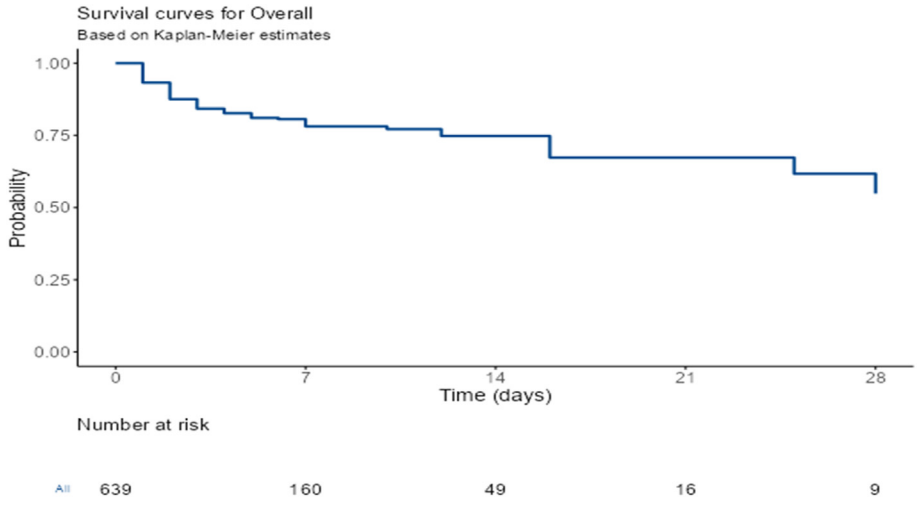

Figure 1: Overall survival (days).

Table 2: Univariate analysis of prognostic factors associated with neonatal mortality in the neonatology department of Agadir, Morocco (N = 639).

Variables	Univariate analysis	
	$_c$HR (95 % CI)	p-value
Reference service:		
Maternity	1	
Emergency	1.60 (1.06−2.43)	**0.025**
Perinatal asphyxia	1.79 (1.24−2.60)	**0.002**
Prematurity	2.20 (1.52−3.17)	**<0.001**
Hemorrhagic syndrome	2.87 (1.86−4.43)	**<0.001**
Hypothermia	9.75 (2.38−39.97)	**0.002**
Neonatal age at admission:		
>7 days	1	
≤7 days	6.99 (1.64−29.76)	**0.008**
Birth weight:		
≥2500 g	1	
<2500 g	2.87 (1.86−4.43)	**<0.001**
Amniotic fluid color abnormality	0.18 (0.03−1.31)	0.09
Jaundice	0.00 (0.00-inf)	0.99

cHR: crude hazard ratio; CI: confidence interval. Significant at p-value ≤ 0.05.

weight, and 28.4 % died. The median age of death was 3 days [2−5]. The main causes of hospitalization were perinatal asphyxia (45.7 %), hemorrhagic syndrome (39.4 %), and prematurity (35.4 %). The details of the descriptive results are shown in Table 1.

Factors associated with survival

Survival analysis indicated that, among the newborns in our study, the overall survival was 93.3 % [91.3−95.2] on the 1st day of life; 78.1 % [74.1−82.3] on the 7th day of life; 74.8 % [69.6−80.3] on the 14th day of life; 67.3 % [58.6−77.4] on the 21st day of life; and 54.8 % [39.9−75.5] on the 28th day of life (Figure 1).

According to univariate analysis, the variables associated with survival were perinatal asphyxia, which increased the risk of death by 79 % ($_c$HR = 1.79, 95 % CI [1.24−2.60], p = 0.002); neonatal age ≤7 days, which multiplied the risk of death by a factor of 7 ($_c$HR = 6.99, 95 % CI [1.64−29.76], p = 0.008); low birth weight or hemorrhagic syndrome, which increased the risk of death ($_c$HR = 2.87 95 % CI 1.86−4.43], p < 0.001); prematurity ($_c$HR = 2.20 95 % CI 1.52−3.17], p < 0.001); emergency department referral, which was associated with a 60 % risk of death ($_c$HR = 1.60 95 % CI [1.06−2.43]; p = 0.025); and hypothermia (cHR = 9.75 95 % CI [2.38−39.97]; p = 0.002) (Table 2 and Figure 2).

In multivariate analysis, the factors indicating poor prognosis were perinatal asphyxia ($_a$HR = 2.61, 95 % CI [1.57−4.43], p < 0.001); prematurity ($_a$HR = 2.15, 95 % CI [1.17−3.94], p = 0.013); neonatal age ≤7 days ($_a$HR = 4.89, 95 % CI [1.14−20.94], p = 0.032); low birth weight ($_a$HR = 2.25, 95 % CI [1.28−3.94], p = 0.005); and hypothermia ($_a$HR = 7.60, 95 % CI [1.71−33.73], p = 0.008) (Table 3).

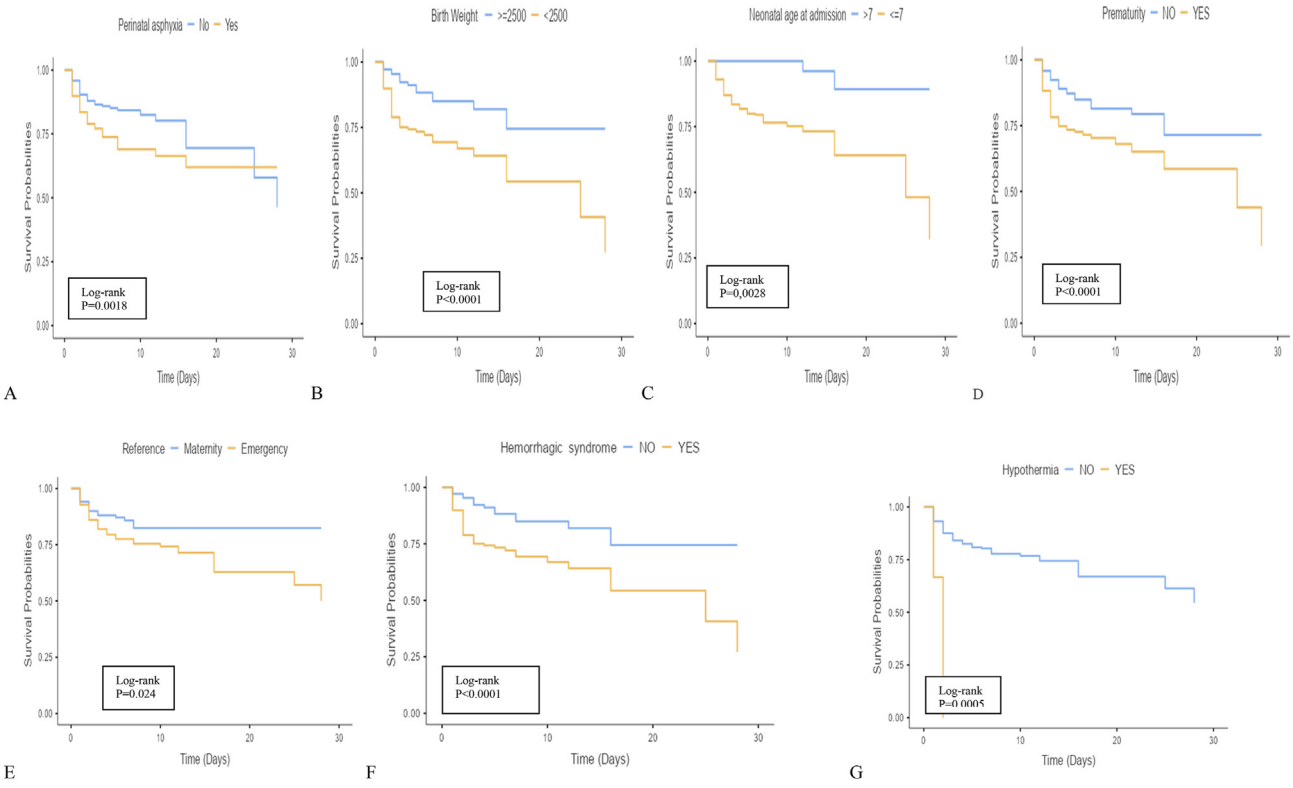

Figure 2: Kaplan–Meier survival curve of significant factors associated with neonatal mortality, determined with log-rank test. A: Perinatal asphyxia. B: Birth weight. C: Neonatal age at admission. D: Prematurity. E: Reference service. F: Hemorrhagic syndrome. G: Hypothermia.

Table 3: Multivariate analysis of prognostic factors associated with neonatal mortality in the neonatology department at Agadir, Morocco (Cox model; N = 639).

Variables	Multivariate analysis	
	$_{a}$HR (95 % CI)	p-value
Reference service:		
Maternity	1	
Emergency	1.41 (0.88–2.24)	0.155
Perinatal asphyxia	2.61 (1.57–4.33)	**<0.001**
Prematurity	2.15 (1.17–3.94)	**0.013**
Hemorrhagic syndrome	NA	NA
Hypothermia	7.60 (1.71–33.73)	**0.008**
Neonatal age at admission:		
≤7 days	4.89 (1.14–20.94)	**0.032**
>7 days	1	
Birth weight:		
<2500 g	2.25 (1.28–3.94)	**0.005**
≥2500 g	1	

aHR: adjusted hazard ratio; CI: confidence interval; NA: not available. Significant at p-value ≤ 0.05.

Discussion

Approximately 4 million babies die during the neonatal period each year.[14] The aim of this research was to examine the characteristics predicting newborn mortality at the neonatology unit of the regional hospital in Agadir, Morocco, in 2022, with a follow-up period lasting as many as 28 days. Halting this mortality and increasing the survival of this vulnerable population can be successful only with a deeper understanding of the elements compromising prognosis in newborns. Therefore, the present study used a retrospective protocol to investigate the characteristics of the cohort.

We present the findings from an examination of 639 cases of newborns younger than 28 days admitted to the neonatology department. The in-hospital MNN rate at Agadir regional hospital was 18 % (95 % CI [15.2–21.2]) between January 1 and May 9 of 2022. A total of 95.9 % of these newborns were hospitalized during their first week of life, and 57.6 % were boys. The average weight of the newborns was 2690 ± 901 g, 39.4 % had low birth weight, and 28.4 % died. The main causes of hospitalization were perinatal asphyxia (45.7 %), hemorrhagic syndrome (39.4 %), and prematurity (35.4 %). The median age at death was 3 days [2–5].

Our results were similar to findings from previous reports, such as the rate of intra-hospital NNM of 19 % in Meknes[15] and the rate of NNM of 19.7 % (95 % CI [10–29]) in Burkina Faso.[16] However, lower rates of NNM have been found in other studies in Togo and Eritrea, which have reported rates of 15.84 % and 6.56 %, respectively.[17,18] Moreover, the NNM rate in one study in Mali was very high, at 31.9 %.[19]

In our study, 98.3 % of deaths (113/115) were recorded during the first week of hospitalization, thus suggesting very high early neonatal mortality, and the risk of death was 78.1 % [74.1–82.3] during the first 7 days of life. Segbedji (2020), Tchagbele (2020), and Demitto (2017) have reached the same conclusion, reporting early neonatal mortality rates

of 88.7 %, 84.4 %, and 76.9 %, respectively.[17,20,21] Indeed, the results of those studies confirm that early neonatal mortality has shown the least progress. Approximately 75 % of newborn deaths occur in the first week of life, and the death rate is extremely high in the first 24 h after birth.[14] This finding is in concordance with our results, in which the risk of death was very high on the first day of life, at 93.3 % [91.3−95.2].

Our study identified several factors associated with poor prognosis in neonatal mortality: perinatal asphyxia ($_{a}$HR = 2.61, 95 % CI [1.57−4.43], p < 0.001); prematurity ($_{a}$HR = 2.15, 95 % CI [1.17−3.94], p = 0.013); neonatal age ≤7 days ($_{a}$HR = 4.89, 95 % CI [1.14−20.94], p = 0.032); low birth weight ($_{a}$HR = 2.25, 95 % CI [1.28−3.94], p = 0.005); and hypothermia ($_{a}$HR = 7.60, 95 % CI [1.71−33.73], p = 0.008).

In countries with very high neonatal mortality rates, the risk of death from asphyxia at birth is multiplied by eight.[14] Additionally, an Apgar score below 7 is statistically associated with neonatal death.[21] In this study, perinatal asphyxia multiplied the risk of death by 2.67. In a study from Marrakech, perinatal asphyxia multiplied the risk of death by a factor of 6.[22] A study in Burkina Faso has also discovered a significant association between the chance of dying and prenatal hypoxia, ranging from 6 to 12 times, depending on the severity of the Apgar score.[23]

Nearly one in four premature babies has circulatory adaptation difficulties in the first 24−48 h of life and has elevated risk of early complications such as intracranial hemorrhage.[24] The risk of death for a baby increases with decreased gestational age, and an inverse relationship is observed between preterm and neonatal mortality. This association has prompted concerns regarding prematurity rates worldwide.[21] The risk of death due to prematurity is three times higher in countries with high neonatal mortality rates than low mortality rates,[14] in line with our findings indicating a higher chance of dying ($_{a}$HR = 2.15, 95 % CI [1.17−3.94], p = 0.013).

Approximately one-third of all babies die on the day of birth, and approximately three-quarters die within the initial week of life.[25] Similarly, in a study in Bamako (Mali), children younger than 7 days were found to have a 92 % risk of dying from their disease compared with older children.[19] In addition, a neonatal age of 1−7 days is significantly associated with elevated risk of death ($_{a}$HR = 4.89, 95 % CI [1.14−20.94], p = 0.032). Therefore, focusing on the critical periods before and immediately after birth is essential to enhance the chances of newborn survival.[1]

A key characteristic of newborns is low birth weight, which is the primary independent predictor of neonatal mortality; evidence has indicated that risk of death increases as birth weight declines.[21] Compared with newborns with normal weight, those with low birth weight have a 3.9 times greater risk of requiring resuscitation at birth.[24] Higher death rates are associated with lower birth weights.[26] In our study, low birth weight was statistically associated with death risk ($_{a}$HR = 2.25, 95 % CI [1.28−3.94], p = 0.005).

Low-weight or ill newborns are most vulnerable to hypothermia, which increases the risk of disease and death in neonates.[27] Our study indicated that hypothermia increased the risk of death 7-fold ($_{a}$HR = 7.60, 95 % CI [1.71−33.73], p = 0.008). Our findings are in agreement with those from a study in Cameroon, in which 68.4 % of newborns who died had hypothermia at admission, and hypothermia was significantly associated with the risk of death (relative risk of 7.2).[28]

Despite efforts to decrease the proportion of babies born underweight, the results have been unsatisfactory.[14] Babies who are born underweight are likely to experience health and development problems, such as learning difficulties; hearing and vision impairment; and chronic respiratory diseases, such as asthma and chronic diseases.[29]

This study's strengths include the use of a retrospective cohort design, which is particularly useful for identifying predictive factors associated with elevated mortality risk. Data reliability was ensured by the absence of loss to follow-up—a major problem in prospective cohort studies. In addition, the large sample size enhanced the study's statistical power. Furthermore, the retrospective design provided a realistic representation of common clinical situations, thus increasing the findings' applicability to standard medical practice. The use of multivariate analysis to adjust for potential confounding factors further strengthened the validity and reliability of the conclusions. This study has the inherent limitations of retrospective studies based on hospital data. Several important variables described in the literature could not be collected, because they were not documented in the medical records. Because of specific constraints, this single center study was limited to a single second-level hospital facility. We acknowledge these limitations and recommend that additional research avenues be investigated to improve understanding of the issues associated with newborn mortality.

Conclusion

Because newborn mortality is a reliable measure of population health and the quality of obstetric and neonatal care, it is a serious public health concern. Better monitoring of pregnancy and good delivery care, with regular monitoring of fetal heart rate, are indispensable for identifying fetuses at risk during labor. Neonatal morbidity and mortality associated with low birth weight, premature birth, and perinatal asphyxia could be decreased or even prevented.

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Conflict of interest

The authors have no conflicts of interest relevant to this article.

Ethical approval

The Ethics Committee of the Faculty of Medicine and Pharmacy in Rabat (Morocco) approved this study (reference number C64-20).

Authors contributions

Conception and design of study: EH, LL, BE, and BA. Acquisition of data: EH. Analysis and/or interpretation of data: EH, LL, BE, and BA. Drafting of the manuscript: EH, LL, YS, BM, EJ, BE, and BA. All authors have read and agreed to the published version of the manuscript. All authors have critically reviewed and approved the final draft, and are responsible for the content and similarity index of the manuscript.

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