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Factors associated with the admission of moderate to late preterm and term neonates within 72 hours of birth at Dedza and Mangochi District Hospitals, Malawi: a matched case-control study

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Abstract

Objective To investigate the demographic characteristics, maternal, and perinatal factors associated with the hospitalization of moderate to late preterm and term neonates within 72 h of birth in the Dedza and Mangochi districts of Malawi.

Methods This case-control study was conducted with one-to-one matching for age, location, and sex. Cases were sick neonates who were admitted in the Sick Intensive Neonatal Care Unit (SINCU) within 72 h of life, while controls were non-sick neonates delivered within two weeks of the birth dates of cases. Prenatal data were extracted from case files, while other maternal practices and demographic characteristics were obtained by interviewing primary care takers or legal guardians after obtaining consent. Descriptive analyses and logistic regression were used to identify factors associated with hospitalization of moderate to late preterm and term neonates within 72 h of birth.

Results Application of tetracycline eye ointment (AOR: 0.41, 95% CI: 0.20–0.82, $p=0.012$) applying chlorhexidine to the umbilical cord stump (AOR: 0.30, 95% CI: 0.10–0.88, $p=0.027$), and stimulation resuscitation (AOR: 0.20, 95% CI: 0.05–0.78, $p=0.020$) were associated with a reduced odd of hospitalization. An increased odds of hospitalization was significantly associated with low birth weight (AOR: 10.48, 95% CI: 4.25–25.89, $p=0.001$), Apgar score < 5 (AOR: 5.0, 95% CI: 2.14–11.63, $p=0.001$), suctioning resuscitation (AOR: 2.82, 95% CI: 1.17–6.83, $p=0.021$), and resuscitation using O_2 (AOR: 4.23, 95% CI: 1.32–13.56, $p=0.015$). Maternal factors associated with reduced odds of hospitalization included the mother testing positive and successfully treated for syphilis antenatally (AOR: 0.06, 95% CI: 0.02–0.18, $p=0.001$) and the mother being married (AOR: 0.39, 95% CI: 0.16–0.93, $p=0.34$). Maternal factors associated with an

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increased odds of hospitalization include premature rupture of membranes (AOR: 2.49, 95% CI: 1.12–5.52, $p=0.025$) and presence of meconium stain during delivery (AOR: 3.14, 95% CI: 1.63–6.06, $p=0.001$).

Conclusion The research findings indicate that several interventions significantly reduce infections in neonates within their initial 72 h of life. These include the application of ophthalmic ointment to all neonates, utilization of chlorhexidine on the umbilical cord stump, and provision of antenatal treatment for syphilis and HIV in infected mothers. Conversely, certain factors increase the likelihood of neonatal morbidity and potential hospitalization during this critical period. These risk factors include low birth weight, a low Apgar score, and conditions necessitating suctioning or oxygen resuscitation at birth. Furthermore, infants born to mothers who experienced premature rupture of membranes or meconium-stained amniotic fluid during parturition are more susceptible to infectious conditions, which may necessitate hospitalization within the first 72 h postpartum. We recommend that stimulation be used as the core procedure for resuscitation, whereas suctioning should be used with caution and only when it is essential. Infection prevention measures should always be adhered to during all procedures on neonates. We recommend intensifying HIV and syphilis testing and treating during the antenatal period to reduce neonatal infection.

Keywords Factors, Hospitalization within 72 h, Neonatal admission, Sick intensive neonatal care unit

Introduction

The first month after birth is the most critical period for the survival of newborns. According to the World Health Organization, in 2021, newborns who died within their first 28 days of life declined from 37 per 1000 live birth in 1990 to 18 in 2021 [1, 2]. In Sub-Saharan Africa, the neonatal mortality rate is the highest worldwide, with 27 deaths per 1000 live births, accounting for 43% of all newborn fatalities reported globally [3]. Malawi, in particular, registers 19 deaths per 1000 live births [1]. According to WHO, despite reducing the Neonatal mortality rate from average of 69 deaths per 1000 live births in 1969 to 19 in 2021 [1], Malawi still faces an urgent need to accelerate progress in neonatal mortality [2, 4].

Since 2000, Malawi has made substantial progress in reducing the neonatal mortality rate, targeting the 2030 Agenda and Sustainable Development Goals which is marked at reducing neonatal deaths to at least as low as 12 per 1000 live birth [5]. However, advances in reducing newborn mortality have been slower than advances in reducing under-five mortality, despite various initiatives [6]. Mortality of babies agedto 59 months has dropped by 54%, from 50 to 23 deaths per 1000 live births [7].

The 2015-16 Malawi Demographic Health Survey report indicated a five year period neonatal mortality rate of 27 deaths per 1000, equating to 1 out of every 37 live births [8]. Conversely, a 2016 UNICEF report cited a neonatal mortality rate of 23.1%, or 1 in every 43 live births [9]. Several factors have been linked to high neonatal mortality in Malawi, including prematurity, intrapartum complications such as birth asphyxia and neonatal encephalopathy, and severe infection [10]. Reports from Sick Neonatal Care Units (SNCUs) suggest that this trend is ongoing. Other studies have also identified the role of out-born births with hypothermia on admission and inadequate monitoring of vital signs, as well as suboptimal management of sepsis, as contributors to increased neonatal mortality [11]. The readmission of term and near-term neonates in the first two weeks of life has also been linked to hyperbilirubinemia and infections as primary reasons for admission [12].

While developing the Malawi Every Newborn Action Plan, a bottleneck analysis outlined areas for improvement to reduce neonatal deaths [13]. Key interventions identified include infection control during and after delivery, ensuring the availability of essential equipment, medicinal supplies, and establishing setups for newborn care in labor wards and nurseries, as well as monitoring and following up neonates after birth [3, 14].

Research in other regions has identified risk factors associated with early morbidity of neonates. In India, maternal risk factors associated with early onset sepsis in neonates included prolonged membrane rupture [15]. In contrast, late onset of sepsis was inversely associated with birth weight and gestational age, leading to increased morbidity and prolonged hospitalization of neonates [16]. In Pakistan, maternal risk factors for neonatal mortality included maternal anemia, maternal malnutrition, grand multi-parity, and poor antenatal care [17].

Research in Malawi has primarily focused on factors contributing to neonatal deaths, with limited studies investigating neonatal hospitalization within 72 h of birth. Given the paucity of data in Malawi, the present study assessed the demographic characteristics and factors associated with hospitalization of neonates within 72 h of birth at the Dedza and Mangochi District Hospitals. This information may prove valuable for policymakers, both locally and beyond, in strengthening the delivery of neonatal health services in Malawi.

Context of this study

While neonatal mortality rates in Malawi have shown little improvement, inpatient neonatal outcomes have improved significantly [18, 19] with the implementation

of interventions such as the bubble Continuous Positive Airway Pressure machine; oxygen supply; interventions such as Helping Baby Breathe, Kangaroo Mother Care, Care of Infant and Newborn, Basic Emergency Obstetric and Newborn Care; and the provision and use of antibiotics. Unpublished data from the Pediatric and Child Health Association in Malawi, which as UNICEF supported neonatal projects in 10 health facilities, confirms the reduction of inpatient neonatal mortality following the implementation of these interventions. For example, in Dedza, inpatient neonatal mortality decreased from 16.3% in 2018 to 12.9% in the 2019. Despite the improvements in survival to discharge, little is known about the factors associated with neonatal admission within the first 72 h of life in developing countries such as Malawi. Therefore, we conducted a case-control study in two districts of Malawi to determine the demographic characteristics and factors associated with neonatal admission within 72 h of birth.

Study setting

The study was conducted in two districts of Malawi, namely Mangochi and Dedza. Both share a boarder with Mozambique. Mangochi, situated in southern Malawi, which is situated on the lakeshore and shares its eastern border with Mozambique, while Balaka and Ntcheu are to the west, Machinga to the south, and Lake Malawi to the north. In 2018, the National Statistical Office (NSO) reported that Mangochi has a population of 1,346,740, which is also mostly young [20]. There are an estimated 309,750 women of child bearing age [21]. Mangochi District Hospital is the main referral hospital in the district, for 34 facilities that offer maternal care. Of these facilities, 15 are Christian Health Association of Malawi (CHAM) facilities.

Geographically, Dedza district covers an area of 3624 km^2 and is located in the central region of Malawi with Mozambique to the west and Lake Malawi to the east. Dedza is bordered by Ntcheu to the south and Lilongwe and Salima to the north. In 2023, the population of Dedza was estimated at 928,487, which is a 20% increase over 2020 estimates [21]. There are an estimated 213,552 women of child bearing age in Dedza. The population is mostly rural and young as demonstrated in the Malawi Demographic Health Survey 2016 report [22].

Dedza District Hospital is the main referral hospital for maternal and child care in the district. The district has 28 health facilities offering maternity services, of which eight are CHAM facilities. Figure 1 shows the locations of the study sites and all the facilities that offer maternal care in the respective districts.

Methodology

Study design and participants

We used a case-control study design, matching cases and controls on a one-to-one basis by sex, location (same traditional authority), and age (within 14 days of birth). The participants comprised infants discharged from SINCUs and postnatal wards at Dedza and Mangochi district hospitals. The districts were selected because they were outstanding in patient numbers among all districts that Pediatric And Child Health Association (PACHA) through funding from UNICEF was supporting to establish SNCUs in Malawi. Cases were neonates who had been admitted to a SINCU within 72 h of birth and then discharged, irrespective of diagnosis (birth asphyxia, prematurity, sepsis, pneumonia, or other congenital abnormalities). All caregivers gave consent. Controls were recruited from neonates who had been discharged from postnatal wards and had never been admitted to a SINCU.

Sample size and sampling technique

The study sought to include all newborns with medical conditions at Dedza and Mangochi district Hospitals. Any neonate discharged from a SINCU was considered eligible for participation, regardless of their health condition. However, infants who stayed in a SINCU for more than 14 days were excluded from the study, as it was not possible to identify suitable age-matched controls for them. The study expected to get 16%of neonates born in both sites to be sick. Therefore, the study aimed to recruit 459 ill neonates over a one-year period, utilizing 90% power, a 0.05 marginal error, and a 10% refusal rate. The intention was to match this with an equal number of healthy neonates, targeting a total sample of 918. However, during the study's implementation, data collection was limited to 423 ill neonates within the year. Furthermore, matching healthy neonates could not be identified for 15 of the ill subjects based on the inclusion criteria. This resulted in an equal sample of 408 for both ill and healthy neonates, totaling 816. The final analysis employed a sample size of 804, following the exclusion of 12 extremely premature infants.

Recruitment plan for participants

All neonates discharged from SINCUs and postnatal wards, with consenting legal guardians, were enrolled in the study. Legal guardians, typically biological mothers who were also primary caretakers, signed informed consent forms before commencing recruitment. After enrolling a sick neonate, the research assistant sought a control in the postnatal unit, matching the neonate by traditional authority, age, and sex. Neonates whose legal guardians declined consent were excluded from the study.

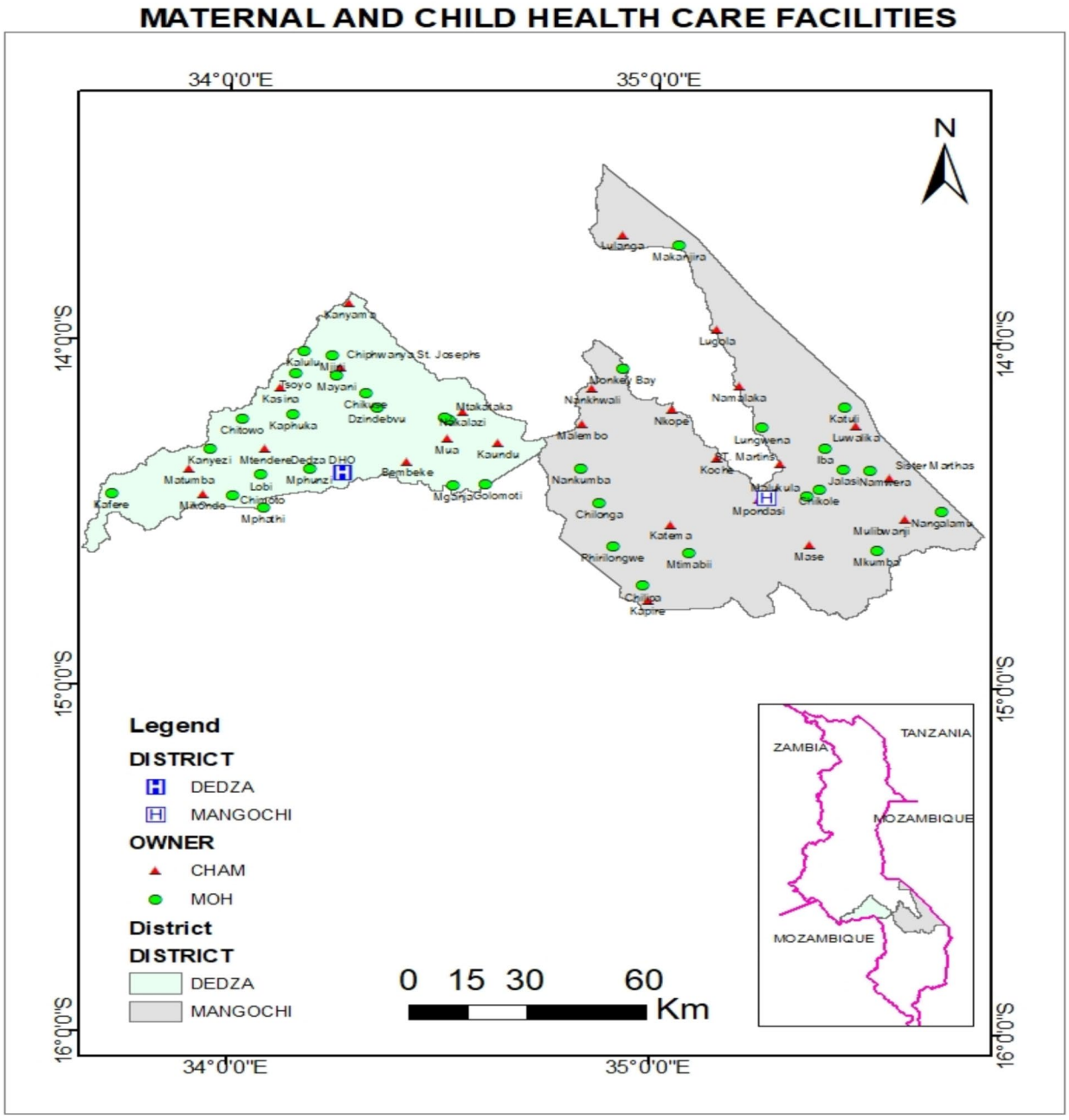

Fig. 1 The location of the Dedza and Mangochi districts where the neonatal matched case-control study was conducted in Malawi
Legend: The study was conducted at two district hospitals, Dedza and Mangochi. These districts were the main referral hospitals for all the maternal and child care in the respective districts. The health facilities offering maternal and child health were categorized into public facilities and Christian Health Association of Malawi (CHAM) facilities

Ethical considerations

We first sought permission to conduct the study from the district commissioners who advised the study team to present the protocol to the District Research Coordinating Committees at the two District Health Offices. The two District Research Committees reviewed the protocol independently. Upon their satisfaction, they issued support letters, which were included in our protocol for ethical review by the National Health Sciences Research Committee (NHSRC). The protocol was approved by the NHSRC under registration number #21/03/2659.

Privacy and confidentiality

All study participants' names were replaced by study ID numbers, and no names were used or shared in any way. Data were securely stored in a password-protected computer, accessible only to investigators. The updated datasets were stored on an external hard drive, also password protected.

Training and pretesting

Twenty nurses and clinicians working in nurseries and postnatal wards underwent a 4-day training program, 10 from each district, including five in the nursery and five in the postnatal ward. The training focused on the study protocol, data collection tools, and the consenting process to ensure standardized data collection. The questionnaires were developed in English and translated into Chichewa. Data collectors were trained in standardized questioning techniques to ensure consistency in the information collected.

We piloted 20 questionnaires, 10 in each district. After piloting, the data were analyzed, and feedback was provided to the data collectors. The tools were then adjusted to incorporate recommendations from the pilot to make the questions more user-friendly.

Data collection

Data collection commenced in May 2021 and ended in May 2022. Data were collected on the day of discharge. Variables collected at discharge included maternal and delivery processes, as well as neonatal characteristics. Data were extracted from patient files and gathered during face-to-face interviews with the mothers or primary care takers. An extraction checklist guide was embedded in the main questionnaire, which captured diverse information not utilized in this analysis, including household socioeconomic status, receipt of health and nutrition services, child morbidity, breastfeeding history, infant and young child feeding knowledge, and physical examination of the child. The majority of the questions employed in this questionnaire were adapted from the Demographic Health Survey questionnaire. Information extracted from patient files which was used in this analysis included birth weight of the neonate, gestational age, mode of delivery, history of premature rupture of membranes, Apgar scores, the need for and type of resuscitation, the presence of a meconium stain during delivery, HIV and syphilis status of the mother, and the provision of routine postnatal interventions such as cleaning the umbilical cord with chlorhexidine, administration of tetracycline eye ointment (TEO), vitamin K, and vaccination with Polio 0 and Bacillus Calmette-Guerin (BCG).

According to Malawian guidelines, all neonates receive intramuscular Vitamin K within the first hour post-partum, with dosage determined by body weight. Infants weighing 1000 g or more are administered 1 mg, whilst those under 1000 g receive 0.5 mg. Additionally, Tetracycline eye ointment is applied as a single dose to the neonate's eyes immediately following delivery. Should these interventions be omitted initially, they may be administered within 24 h of birth.

In cases of preterm labour in its early stages, pregnant women are typically administered dexamethasone 6 mg intramuscularly every 12 h for a 48-hour period. If the woman presents with established labour, a 24-hour course of 12 mg dexamethasone intramuscularly is administered. In situations where dexamethasone is unavailable, betamethasone 12 mg IM is provided once daily for 48 h.

Additionally, we recorded the mother's age at her first pregnancy and measured the neonate's length and head circumference. We also recorded the marital status of the biological mother, occupation of the head of household, and education level of the biological mother. Data were collected electronically and uploaded daily via a Wi-Fi network to a Kobo project server database.

Data management

Rigorous data collection and management procedures were implemented to ensure high data quality. We designed electronic data tools with proper restrictions to prevent data collectors from entering irrelevant data, and skip patterns were built into the system. Each week, records were reviewed, and data were verified for accuracy and completeness. Data cleaning was carried out in STATA.

Data analysis

Data were imported to STATA [23] for cleaning and analysis. Categorical variables were summarized using summary statistics and frequency tables. For continuous variables, data were summarized using means and standard deviations (SDs) for normally distributed data and medians and interquartile ranges for skewed data. A multicollinearity diagnostic test was conducted to establish independence (variance inflation factor <10, tolerance level <0.1) of the explanatory variables before they were included in the model. We also examined interaction variables before including them in the model. We used Chi-square tests of association to assess categorical dependent variables using $p=0.05$ and 95% confidence interval (CI) as the threshold for significance. Most of the variables had less than 5% missing data. However, education level of the mother and Syphilis results of the mother had above 10% missing data. The sample size was large enough for records with missing data to be excluded from the analysis of the particular variables. As a rule of thumb, a minimum of 10 cases with the least frequent outcome for each explanatory variable in

a regression model is required. Chi square tests require that the expected frequency for each category be not less than 5. The sample collected was adequate to meet these conditions.

Our independent variable was neonatal health outcome within 72 h of birth, categorized as either neonates who had gone through SINCU or those who had been in a normal postnatal ward. Predictor variables included demographic data, maternal variables (e.g. parity, gestational age, premature rupture of membranes, presence of meconium, HIV and syphilis status of the mother, occupation of the household head), clinical condition of the neonate, and resuscitation measures.

We also included variables such as Apgar score and gestational age into the analysis. Apgar scores were categorized as low (1–4), moderate fair (5–7), or good (8–10). In terms of gestational age, babies born alive before 37 weeks of pregnancy is complete [24] are considered preterm, however, in this study we only analyzed data for moderate to late preterm gestation which was marked as 32 to < 37 weeks, 37 to 41 weeks as term gestation, and 42 weeks and above were treated as post-term pregnancies.

The study employed univariable and multivariable logistic regression analysis to assess associations. The outcomes of interest were neonatal outcomes within 72 h of birth; whether the participant was admitted due to sickness (case) or discharged home without being sick (controls). A backward hierarchical stepwise approach was employed in the multivariate regression, with variables with a $p<0.25$ included in the initial model. Non-significant variables were sequentially excluded until the final model was reached. The most appropriate final model was chosen based on the lowest Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) [25].

Results

The study enrolled 831 neonates over the course of one year. However, 15 cases were dropped because we could not match suitable controls within 14 days of birth. Twelve study participants were not included in this analysis because their birth weight and gestation age was below 1500 g and < 32 weeks respectively [24] which is deemed early preterm neonates. Our final sample included 804 neonates, comprising 397 cases and 407 controls. Among the neonates, 472 (58.71%) were male sex and 332 (41.29%) were female sex. Primary reasons for hospitalization were birth asphyxia ($n=143$), neonatal sepsis ($n=90$), other conditions ($n=62$, including staphylococcus scalded skin syndrome, conjunctivitis, abscesses, orthopedic conditions, neonatal jaundice, prematurity ($n=44$), respiratory distress syndrome ($n=20$), pneumonia ($n=16$), meconium aspiration ($n=13$), and congenital abnormalities including gastroschisis ($n=3$).

The mean weight of all the babies was 2932.31 g (SD 540.88, range: 1500–5300 g). Mean maternal age at first delivery was 19.02 years (SD 2.52, range: 13–30 years) as shown in Table 1. Just over half of neonates were recruited from Mangochi (52.99%, $n=426$), whilst 47.01% ($n=378$) were recruited from the Dedza district (Table 2). Almost all neonates were delivered at health facilities (cases: 98.22%, $n=396$; controls: 99.51%, $n=403$). More neonates in the case group were resuscitated during delivery (67.76%, $n=269$) than neonates in the control group (30.71%, $n=125$).

Most of the neonates were delivered via spontaneous vaginal delivery (81.55%, $n=641$). However, all neonates delivered in the breech position (2.60%, $n=10$) and those delivered through vacuum extraction (2.86%, $n=11$) belonged to the case group.

We observed that Polio and BCG vaccine, including Vitamin K, were administered more frequently to controls than to cases. Specifically, 31.92% ($n=128$) of controls received the Polio vaccine, while only 11.86% ($n=46$) of cases received the vaccine. A similar trend was observed for the BCG vaccine, with 35.75% ($n=143$) of controls receiving the vaccine, while only 15.46% ($n=60$) of cases received the vaccine. Though the differences were minimal, more controls than cases received Vitamin K (34.65%, $n=140$ versus 23.59%, $n=92$).

Interestingly, more mothers of neonates in the control group tested syphilis reactive ($n=60$) than mothers of neonates in the case group ($n=4$).

Table 1 Characteristics of late preterm and term neonates who were admitted to Dedza and Mangochi District hospitals, Malawi, May 2021 to May 2022

Variable	Observation ($n=804$)	Mean	SD	Min	Max
Birth weight (g)	797	2932.31	540.88	1500	5300
Gestation age (weeks)	800	37.11	2.02	32	44
Apgar score at 1 min (scores)	751	7.32	1.88	1	10
Apgar score at 5 min (scores)	751	9.25	1.47	3	10
Age of mother at first delivery (years)	730	19.02	2.52	13	30
Length of the neonate at discharge (cm)	607	47.32	4.87	18	64.5
Head circumference at discharge (cm)	610	35.17	2.72	26.3	50

SD, standard deviation

Table 2 Descriptive characteristics of the late preterm and term neonates delivered at Dedza and Mangochi District Hospitals

Variable	Controls	Cases	Total	*P*-value
Total	**407 (50.62%)**	**397 (49.38%)**	**804 (100%)**	
District of birth (n [%])			*n* = 804	**0.927**
Mangochi	215 (52.83)	211 (53.15)	426 (52.99)	
Dedza	192 (47.17)	186 (46.85)	378 (47.01)	
Gender by birth (n [%])			*n* = 804	**0.893**
Female	169 (41.52)	163 (41.06)	332 (41.29)	
Male	238 (58.48)	234 (58.94)	472 (58.71)	
Mode of delivery			*n* = 786	**0.001**
Spontaneous vaginal delivery	351 (87.31)	290 (75.52)	641 (81.55)	
Breech delivery	0 (0.00)	10 (2.60)	10 (1.27)	
Caesarian section	51 (12.69)	73 (19.01)	124 (15.78)	
Vacuum extraction	0 (0.00)	11 (2.86)	11 (1.40)	
Presence of meconium stain on delivery			*n* = 773	**0.001**
Not present	359 (91.35)	292 (76.84)	651 (84.22)	
Present	34 (8.65)	88 (23.16)	122 (15.78)	
Place of birth			*n* = 798	**0.176**
Home/in-transit	2 (0.49)	7 (1.78)	9 (1.13)	
Health facility	403 (99.51)	396 (98.22)	789 (98.87)	
HIV status of the neonate			*n* = 788	**0.340**
None-exposed	350 (87.06)	346 (89.64)	696 (88.32)	
Exposed and mother on HAART	26 (6.47)	16 (4.15)	42 (5.33)	
Unknown	26 (6.47)	24 (6.22)	50 (6.35)	
Marital status of mother			*n* = 796	**0.302**
Single	26 (6.44)	42 (10.71)	68 (8.54)	
Married	366 (90.59)	337 (85.97)	703 (88.32)	
Separated	5 (1.24)	5 (1.28)	10 (1.26)	
Divorced	6 (1.49)	7 (1.79)	13 (1.63)	
Widowed	1 (0.25)	1 (0.26)	2 (0.25)	
Occupation of household head			*n* = 798	**0.001**
None	236 (58.27)	295 (75.06)	531 (66.54)	
Business	67 (16.54)	40 (10.18)	107 (13.41)	
Farmer	85 (20.99)	49 (12.47)	134 (16.79)	
Permanent or civil servant	17 (4.20)	9 (2.29)	26 (3.26)	
Education level of the mother			*n* = 678	**0.248**
Primary level	271 (76.77)	231 (71.08)	502 (74.04)	
Secondary level	71 (20.11)	84 (25.85)	155 (22.86)	
College/Technical/University	11 (3.11)	10 (3.08)	21 (3.10)	
Applied chlorhexidine on umbilical cord			*n* = 797	**0.001**
No	38 (9.36)	73 (18.67)	111 (13.93)	
Yes	368 (90.64)	318 (81.33)	686 (86.07)	
Applied tetracycline eye ointment (TEO)			*n* = 790	**0.215**
No	225 (55.69)	198 (51.30)	423 (53.54)	
Yes	179 (44.31)	188 (48.70)	367 (46.46)	
Resuscitation conducted during birth			*n* = 804	**0.001**
No	282 (69.26)	128 (32.24)	410 (51.0)	
Yes	125 (30.71)	269 (67.76)	394 (49.14)	
Given Vitamin K			*n* = 794	**0.001**
No	264 (65.35)	298 (76.41)	562 (70.78)	
Yes	140 (34.65)	92 (23.59)	232 (29.22)	
Given Polio vaccination			*n* = 789	**0.001**
No	273 (68.08)	342 (88.14)	615 (77.95)	
Yes	128 (31.92)	46 (11.86)	174 (22.05)	
Given BCG vaccination			*n* = 788	**0.001**

Table 2 (continued)

Variable	Controls	Cases	Total	*P*-value
No	257 (64.25)	328 (84.54)	585 (74.24)	
Yes	143 (35.75)	60 (15.46)	203 (25.76)	
Premature rupture of membrane			*n* = 770	**0.001**
No	367 (93.15)	294 (78.19)	661 (85.84)	
Yes	17 (4.31)	43 (11.44)	60 (7.79)	
Don't know	10 (2.54)	39 (10.37)	49 (6.36)	
Syphilis results of the mother			*n* = 446	**0.001**
Non-reactive	161 (65.84)	188 (92.61)	348 (78.03)	
Reactive and treated	60 (24.69)	4 (1.97)	64 (14.35)	
Not done	23 (9.47)	11 (5.42)	34 (7.62)	
Stimulation resuscitation measure			*n* = 394	**0.001**
No	4 (3.20)	58 (21.56)	62 (15.74)	
Yes	121 (96.8)	211 (78.44)	332 (84.26)	
Suctioning resuscitation measure			*n* = 394	**0.001**
No	105 (84.0)	130 (48.33)	235 (59.64)	
Yes	20 (16.0)	139 (51.67)	159 (40.36)	
Bulb valve and mask resuscitation			*n* = 394	**0.001**
No	116 (92.80)	186 (69.14)	302 (76.65)	
Yes	9 (7.20)	83 (30.86)	92 (23.35)	
O_2resuscitation			*n* = 394	**0.001**
No	117 (93.6)	151 (56.13)	268 (68.02)	
Yes	8 (6.40)	118 (43.87)	126 (31.98)	

Table 3 presents the stepwise multivariable regression results. Neonatal factors protective against hospitalization included applying tetracycline to newborns' eyes within 48 h (Adjusted Odds Ratio 0.41, CI 95%: 0.20–0.82, $p=0.012$), applying chlorohexidine to the umbilical stump (AOR 0.30, CI 95%: 0.18–0.88), $p=0.027$), and conducting stimulation resuscitation (AOR 0.20, CI 95%: 0.05–0.78, $p=0.020$). Neonatal factors that increased the risk of hospitalization included low birth weight (AOR 10.48, CI 95%: 4.25–25.89, $p=0.001$), 1 min Apgar score between 4 and 7 (AOR 5.00, CI 95%: 2.14–11.63, $p=0.001$), and resuscitation with O_2 (AOR 4.23, CI 95%: 1.32–13.56, $p=0.015$).

Table 4 presents maternal factors associated with the admission of neonates within their first 72 h of life. Maternal factors that increased the risk of hospitalization included premature rupture of membranes (PROM) (AOR 2.49, CI 95%: 1.12–5.52, $p=0.025$). Similarly, neonates had a higher risk of being admitted if their mothers had an unknown history of PROM (AOR 18.74, CI 95%: 2.46–143.08, $p=0.005$). Neonates had a higher risk of being admitted if the mother reported having meconium during delivery (AOR 3.14, CI 95%: 1.63–6.06, $p=0.001$). In this study, mode of delivery, gestational age at birth, occupation, and education level of the mother were not associated with admission within 72 h of delivery. Maternal factors that were protective against hospitalization included the mother being married (AOR: 0.39, CI 95%: 0.16–0.93, $p=0.034$). Surprisingly, babies had a smaller risk of being admitted if their mothers had tested positive for syphilis and successfully treated during the antenatal period (AOR: 0.06, CI95%: 0.02–0.18, $p=0.001$).

Discussion

This study used a one-to-one matched prospective case-control study design to identify factors associated with the hospitalization of neonates within 72 h of birth in Malawi. In this setting, factors associated hospitalization included low birth weight, low Apgar score, and resuscitation with O_2. Protective factors against hospitalization included infection prevention measures such as applying tetracycline and cleaning the umbilical stump with chlorhexidine. Our findings support the importance of good antenatal care and infection prevention measures to prevent infant morbidity.

This study found that, applying tetracycline to every newborn immediately after birth was significantly protective against hospitalization in the first 72 h of life. According to the World Health Organization, neonates can contract infections in the birth canal [26]. tetracycline can be used as a prophylactic to prevent eye infections in newborns [26–28]. Bell et al. in their study conducted in USA [29] suggested that vaginal delivery may promote the transmission of chlamydia trachomatis from infected mothers to newborns. In our study, infection control in the form of using chlorhexidine to clean the umbilical stump was also protective against hospitalization. This is supported by a systematic review of high

Table 3 Neonatal factors associated with hospitalization of late preterm and term neonates within 72 h of life at Dedza and Mangochi districts, Malawi

Variable		Univariable Analysis		Multi-variable analysis			
				Initial model		Final model	
		Crude Odds (95% CI)	*P*-value	AOR (95% CI)	*P*-value	AOR (95% CI)	*P*-value
Tetracycline eye ointment	**Not given ref**	**1**		**1**		**1**	
	Given	1.19 (0.90–1.58)	0.216	0.39 (0.17–0.87)	0.021	0.41 (0.20–0.82)	0.012
Chlorhexidine applied	**Not applied ref**	**1**		**1**		**1**	
	Applied	0.45 (0.30–0.68)	0.001	0.28 (0.10–0.84)	0.022	0.30 (0.10–0.88)	0.027
Polio vaccination given	**Not given ref**	**1**		**1**		**1**	
	Given	0.29 (0.20–0.42)	0.001	0.54 (0.16–1.78)	0.310	0.58 (0.18–1.89)	0.368
BCG vaccination given	**Not given ref**	**1**		**1**		**1**	
	Given	0.33 (0.23–0.46)	0.001	0.20 (0.07–0.59)	0.003	0.20 (0.07–0.57)	0.003
Birthweight categories	**Normal birthweight ref**	**1**		**1**		**1**	
	Low birthweight	3.64 (2.49–5.33)	0.001	10.30 (4.04–26.27)	0.001	10.48 (4.25–25.89)	0.001
Apgar score at 1 min	**High scores (8–10) ref**	**1**		**1**		**1**	
	Medium score (5–7)	7.43 (5.11–10.80)	0.001	5.24 (2.23–12.29)	0.001	5.00 (2.14–11.63)	0.001
	Low score (1–4)	46.72 (18.52–117.84)	0.001	3.27 (0.55–19.67)	0.195	3.17 (0.53–18.94)	0.205
Apgar score at 5 min	**High scores (8–10) ref**	**1**		**1**		**1**	
	Medium score (5–7)	43.44 (13.59–138.85)	0.001	3.79 (0.67–21.59)	0.133	3.76 (0.67–21.12)	0.133
	Low Score (1–4)	Empty		Empty		Empty	
Stimulation resuscitation	**Not done ref**	**1**		**1**		1	
	Done	0.12 (0.04–0.34)	0.001	0.19 (0.05–0.77)	0.02	0.20 (0.05–0.78)	0.020
Suctioning resuscitation	**Not done ref**	1		1		1	
	Done	5.61 (3.29–9.58)	0.001	2.91 (1.20–7.07)	0.018	2.82 (1.17–6.83)	0.021
Bag/valve and mask resuscitation	**Not done ref**	1		1		1	
	Done	5.75 (2.78–11.89)	0.001	0.39 (0.11–1.37)	0.142	0.39 (0.11–1.37)	0.140
O_2 resuscitation	**Not done ref**	1				1	
	Done	11.43 (5.37–24.33)	0.001	4.29 (1.33–13.78)	0.015	4.23 (1.32–13.56)	0.015
Vitamin K given	**Not given ref**	**1**		**1**			
	Given	0.58 (0.43–0.79)	0.001	1.05 (0.43–2.55)	0.911		

quality evidence showing that the use of chlorhexidine in newborn umbilical cord care reduces mortality and omphalitis/infection [30]. Since infection was one of the main causes of hospitalization in our study, preventing infection is likely to play large role in reducing morbidity.

We found that more neonates in the control group received the Polio O and BCG vaccines than those neonates who were admitted within 72 h of their birth. This discrepancy may be attributed to vaccination practices in Malawian hospitals where only otherwise well infants are vaccinated at discharge. Ensuring that neonates who are admitted to SINCUs receive vaccinations before discharge should be a priority.

In our study, low or moderate Apgar scores were associated with hospitalization of neonates within the first 72 h of life. Previous studies have reported that lower Apgar scores are associated with higher mortality, while infants with higher Apgar scores have better outcomes [31]. Low Apgar scores (<4) are associated with developing a number of health conditions, such as birth asphyxia leading to cerebral palsy in the long term [32], which may lead to admission within the first 72 h of life. Greenough et al. in their study conducted in United Kingdom further reported that low Apgar scores are associated with elevated levels of catecholamine and acidosis [33], as a result of birth asphyxia that may lead to several adverse clinical outcomes, which may require admission to a SINCU [34]. Additionally, low birth weight is associated with an increased odds of neonates being hospitalized within 72 h of life [35].

Furthermore, we found that neonates resuscitated using stimulation had lower odds of admission, while those neonates resuscitated with suctioning and O_2 had higher odds of admission. This suggests that the severity of the hypoxia may play a role, with mild asphyxia responding well to stimulation and more severe cases requiring oxygen and suctioning. In contrast to more invasive procedures, babies can be resuscitated using stimulation, which can simply encompass rubbing spine to stimulate breathing. Invasive procedures, such as suctioning, can result in the baby being admitted for further monitoring. Suctioning is quite invasive, involving the insertion of tubes, and may be a risk factor for infection if not properly done. Suctioning may also damage the

Table 4 Maternal factors associated with hospitalization of later preterm and term neonates within 72 h of life in Dedza and Mangochi districts, Malawi

Variable		Univariable analysis		Multi-variable analysis			
				Initial model		Final model	
		Crude Odd (95% CI)	*P*-value	AOR (95% CI)	*P*-value	AOR (95% CI)	*P*-value
HIV-STATUS of the neonate	**Non-exposed ref**	**1**		**1**		**1**	
	Exposed	0.62 (0.33–1.18)	0.147	0.7 (0.01–0.87)	0.039	0.30 (0.09–0.998)	0.050
	Unknown	0.93 (0.53–1.66)	0.815	0.51 (0.10–2.51)	0.409	0.55 (0.17–1.77)	0.317
Premature rupture of membrane	**Not ruptured ref**	**1**		**1**		**1**	
	Yes Raptured	3.16 (1.76–5.65)	0.001	4.63 (1.35–15.91)	0.015	2.49 (1.12–5.52)	0.025
	Unknown	4.87 (2.39–9.92)	0.001	Empty		18.74 (2.46–143.08)	0.005
Syphilis test results	**Non-reactive**	**1**		**1**		**1**	
	Reactive & treated	0.06 (0.02–0.16)	0.001	0.06 (0.01–0.29)	0.001	0.06 (0.02–0.18)	0.001
	Not tested	0.40 (0.19–0.86)	0.019	0.63 (0.17–2. 32)	0.486	0.50 (0.22–1.15)	0.102
Meconium present	**Not observed ref**	**1**		**1**		1	
	Yes Observed	3.18 (2.08–4.87)	0.001	5.36 (1.77–16.73)	0.003	3.14 (1.63–6.06)	0.001
Marital status	**Single ref**	1		1		1	
	Married	0.57 (0.34–0.95)	0.031	0.22 (0.07–0.74)	0.014	0.39 (0.16–0.93)	0.034
	Separated	0.62 (0.16–2.35)	0.481	0.63 (0.03–14.35)	0.772	0.51 (0.06–4.25)	0.537
	Divorced	0.72 (0.22–2.39)	0.594	0.62 (0.05–7.37)	0.702	0.43 (0.07–2.69)	0.368
	Widowed	0.62 (0.04–10.33)	0.738	Empty		Empty	
Education level	**Primary level ref**	1		1			
	Secondary level	1.39 (0.97–1.99)	0.075	1.67 (0.78–3.60)	0.188		
	College/Technical	1.17 (0.48–2.87)	0.726	6.54 (0.96–44.41)	0.055		
	University	Empty		Empty			
Occupation	**No occupation ref**	1		1			
	Business	0.48 (0.31–0.73)	0.001	0.80 (0.33–1.96)	0.628		
	Farming	0.46 (0.31–0.68)	0.001	1.01 (0.40–2.55)	0.978		
	Permanent work	0.42 (0.19–0.97)	0.041	0.20 (0.03–1.18)	0.076		
Given steroids if premature labor started	**Not administered ref**	1		1			
	Yes administered	7.72 (2.24–26.51)	0.001	5.23 (0.38–71.42)	0.307		
	Unknown	10.29 (3.59–29.51)	0.001	19.71 (2.39–62.78)	0.005		
Gestation age of the pregnancy	**Term (37–41 weeks) ref**	**1**		**1**			
	Moderate to late Pre-term (between 32 to < 37 weeks)	1.66 (1.20–2.31)	0.002	0.94 (0.46–1.94)	0.879		
	Post-term (42 weeks and above)	0.66 (0.19–2.29)	0.518	0.18 (0.01–3.52)	0.256		
Mode of delivery	**Normal delivery (SVD) Ref**	**1**		**1**			
	Breech delivery	**Empty**		**0**			
	Caesarean Section	**1.73 (1.17–2.56)**	**0.006**	**0.71 (0.32–1.57)**	0.404		
	Vacuum extraction	Empty		0			

delicate skin of the neonate, which may result in open wounds and cause the entry of microorganisms. In our study, babies resuscitated with O_2 also had a higher odds of admission which is consistent with other studies, since these babies may suffer from respiratory problems, which are a major cause of hospitalization [36].

Maternal factors were also explored, with PROM being identified as a significant risk factor for neonatal admission. PROM increases the risk of infection and preterm labor [37], which exacerbates vulnerability to infection and other adverse birth outcomes. Previous studies have reported increased mortality rates of neonates born after PROM [38]. In Bangladesh and elsewhere, PROM has also been associated with increased incidence of infectious diseases, respiratory distress syndrome, birth asphyxia, and fetal distress [39, 40].

Another maternal factor associated with neonatal admission was the presence of meconium in the amniotic fluid during labor. During delivery, neonates can easily aspirate the meconium-stained amniotic fluid, which may cause infection and other respiratory disorders that require admission. The presence of meconium-stained amniotic fluid is associated with neonatal morbidity and mortality [41]. The presence of meconium-stained fluid

has been associated with fetal hypoxia, seizure, cerebral palsy, and meconium aspiration syndrome [42].

Interestingly, we found that married mothers had reduced odds of giving birth to a neonate who required hospitalization. Various factors might explain this observation. Married mothers may receive better social, psychological, and financial support during pregnancy. Most of the mothers in our study were poorly educated and household heads were unemployed or without a source of income. This may lead to maternal malnutrition, impacting birth outcomes. This intriguing result warrants further investigation. Additionally, mothers who tested positive for syphilis had reduced odds of their babies being hospitalized. Usually, we expect that neonates born from these mothers would contract the infection from their mothers and require hospitalization. The fact that these mothers receive good health education and treatment during the antenatal period suggests that they had good antenatal care, protecting their babies from acquiring infections. According to the World Health Organization, mothers are required to receive treatment before delivery, which protects newborn babies [26]. This finding agrees with the study done in Switzerland by Meyer et al., which reported one newborn infected out of 8, after the syphilis positive mothers were adequately treated of Syphilis during the pregnancy [43].

Limitations

In this study, both univariable and multivariable logistic regression analysis were conducted. Ideally, the power of our study would be enhanced if we had more than one control per case, however our sample size was adequate. We observed that, education of the mother and syphilis status of the mother had more than 10% missing data. Therefore, their results should be interpreted consciously. The two sampled hospitals are from semi-urban location which do not represent the rural setting of Malawi, however the facilities were the only referral hospitals in the respective districts. The utilization of questionnaires that require participants to recollect information in specific domains may introduce recall bias. However, in this analysis, the majority of data was obtained from patient records documented contemporaneously, thereby minimizing the likelihood of recall bias. Although the use of extracted data might potentially result in information omission, the data collection process occurred immediately following discharge on hospital premises. This allowed data collectors to consult additional sources such as patient health passports and hospital registers, when necessary, variables were absent from patient files.

Conclusion

In summary, this study identified various maternal and neonatal factors associated with newborn hospitalization within 72 h of birth at Dedza and Mangochi district hospitals. Prophylactic measures against infection, such as the application of tetracycline eye ointment to neonates and the use of chlorhexidine for umbilical cord care, were found to reduce the likelihood of hospitalization. Infants who required only stimulation for resuscitation also demonstrated lower odds of admission. Conversely, neonates with moderate or low Apgar scores, low birth weight, or those requiring suctioning and oxygen resuscitation exhibited higher probabilities of admission. Mothers who were married or had received treatment for syphilis following a positive test were less likely to have their newborns admitted. These findings suggest that mothers receiving appropriate support, including early treatment and antenatal education, are more likely to experience fewer adverse pregnancy and perinatal outcomes [44, 45]. Further research is necessary to examine the impact of socio-economic factors on reducing admission rates within 72 h of birth. The Malawian government should enhance the provision of Polio 0 and BCG vaccines to all newborns through the implementation of appropriate systems. Furthermore, the use of eye ointments and chlorhexidine for cord care should be promoted in hospitals. When resuscitating newborns, stimulation should be the preferred method, while suctioning should be employed judiciously.

Supplementary Information

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Supplementary Material 1

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Author contributions

PLH conceptualized and designed the study, supervised data collection, conducted data analysis, interpreted results, and prepared the draft manuscript. LD analyzed data, interpreted results, and reviewed and edited the manuscript. CSC prepared and drafted the first manuscript, interpreted results, and reviewed and edited the final manuscript. LT analyzed data, interpreted results, and reviewed and edited the manuscript. EM conceptualize the study, supervised data collection, contributed in study design, interpreted results, and reviewed and edited the manuscript.

BM reviewed and edited the manuscript. GEM reviewed and edited the manuscript. JRC interpreted results and reviewed and edited the manuscript. MS interpreted results and reviewed and edited the manuscript. CN interpreted results and reviewed and edited the manuscript. NL helped to conceptualize the study, supervised data collection, designed the study, and reviewed and edited the manuscript. FG helped to conceptualize and provided oversight on the study and edited the final manuscript. TDH helped to conceptualize the study, helped in study design, provided oversight on the study, reviewed and edited the final manuscriptAll the authors have read and agree with the final draft of the manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by National Health Sciences Research Committee (NHSRC) under registration number #**21/03/2659**. Written informed consent was sought from the legal guardians before the neonate was enrolled.

Competing interests
Upon reviewing the journal's guidelines, it is noted that the following authors of this manuscript have disclosed competing interests: Jacqueline Rose. Chinkonde, Mesfin Senbete, Charles Nwosisi, Fatima Gohar and Tedbabe D. Hailegebriel are affiliated with UNICEF as employees. The remaining authors have stated that they have no conflicting interests to declare.

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