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Original article

Congenital Anomalies and their Outcomes in the Neonate Intensive Care Unit in Misurata Center

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ABSTRACT

Background and objective. *Congenital anomalies are a significant cause of infant morbidity and mortality. This study examined the prevalence, types, and associated risk factors of congenital anomalies and their outcomes in infants admitted to the Neonatal Intensive Care Unit (NICU) of Misurata Hospital, Libya, from January to December 2022.* ***Methods.*** *A retrospective review of medical records of infants with congenital anomalies admitted to the NICU of Misurata Hospital from January to December 2022 was conducted. Data on demographics, clinical presentation, maternal factors, and outcomes were collected. Descriptive and statistical analyses were performed.* ***Results.*** *A total of 53 infants with congenital anomalies were included. The mortality rate was 34%. The most prevalent anomalies were congenital heart defects, hypospadias, cleft lip and palate, hydrocephalus, and syndromic baby. Cesarean section, sepsis, maternal age over 35 years, high parity, polyhydramnios, diabetes mellitus, and oligohydramnios were associated with increased risk of mortality or congenital anomalies.* ***Conclusions.*** *Congenital anomalies pose a substantial burden on neonatal health in this setting. Cesarean section, sepsis, and specific maternal factors were identified as risk factors. These findings underscore the importance of tailored care for mothers and infants with congenital anomalies to improve outcomes.*

Keywords: Congenital Anomalies, Neonatal Intensive Care Unit, Mortality, Risk Factors, Libya

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الخلفية والهدف. التشوهات الخلقية هي سبب مهم لمرض ووفيات الرضع. فحصت هذه الدراسة انتشار وأنواع وعوامل الخطر المرتبطة بالتشوهات الخلقية ونتائجها لدى الرضع الذين تم إدخالهم إلى وحدة العناية المركزة لحديثي الولادة في مستشفى مصراتة، ليبيا، من يناير إلى ديسمبر 2022. **طرق الدراسة**. أجريت مراجعة بأثر رجعي للسجلات الطبية للرضع الذين يعانون من تشوهات خلقية تم إدخالهم إلى وحدة العناية المركزة لحديثي الولادة في مستشفى مصراتة من يناير إلى ديسمبر 2022. تم جمع البيانات عن التركيبة السكانية والعرض السريري والعوامل الأمومية والنتائج. تم إجراء التحليلات الوصفية والإحصائية. **النتائج**. تم تضمين ما مجموعه 53 رضيعًا يعانون من تشوهات خلقية. كان معدل الوفيات 34٪. كانت أكثر التشوهات انتشارًا هي عيوب القلب الخلقية، ونقص تنسج القضيب، والشفة والحنك المشقوقين، واستسقاء الرأس، والطفل المتلازمي. ارتبطت الولادة القيصرية، وتسمم الدم، وعمر الأم فوق 35 عامًا، وارتفاع معدل الولادات، وزيادة السائل الأمنيوسي، ومرض السكري، وقلة السائل الأمنيوسي بزيادة خطر الوفاة أو التشوهات الخلقية. **الاستنتاجات**. تشكل التشوهات الخلقية عبئًا كبيرًا على صحة الأطفال حديثي الولادة في هذا الوضع. تم تحديد الولادة القيصرية، وتسمم الدم، وعوامل أمومية محددة كعوامل خطر. تؤكد هذه النتائج على أهمية الرعاية المخصصة للأمهات والأطفال الذين يعانون من تشوهات خلقية لتحسين النتائج.

INTRODUCTION

Congenital anomalies (CA) are conditions of prenatal origin that are present at birth and may have an impact on an infant's health, development, and/or survival. They are also widely referred to as birth defects, congenital diseases, congenital malformations,

or congenital abnormalities. A vast range of anatomical and functional abnormalities are referred to as congenital anomalies, and they can manifest as a single defect or as a group of defects [1].

There are two categories of congenital anomalies: major and minor anomalies. Major anomalies are structural alterations that usually demand medical intervention and have a significant impact on the affected infant's social, medical, surgical, or cosmetic outcomes. Anencephaly, cardiac abnormalities, spina bifida, and orofacial clefts are a few examples. The majority of congenital anomaly-related death, morbidity, and disability are caused by this category of anomalies. In the other hand, Minor anomalies are structural alterations posing little to no risk to health and typically have minimal social or cosmetic effects. Identifying syndromes can be aided by minor anomalies, which are more prevalent than major anomalies. A single palmar crease and clinodactyly are two examples of minor anomalies [2].

Major anomalies affect 2-4% of livebirths [3], causing 8–16% of newborn deaths [4] of which 70% of pass away in the first month of life [5]. According to a World Health Organization (WHO) estimate, 3 million infants are born with serious CA every year, of which about one fifth are severe and life threatening. [6]. Prevalence of congenital anomalies has remained unchanged. Nonetheless, the risk for various malformations varies and may be associated with genetic predispositions, in addition to cultural and societal distinctions that may impact exposures, e.g cultural diets with low folic acid causing folic acid deficiency causes higher incidence of neural tube abnormalities [7].

Genetic or chromosomal abnormalities, exposure to specific drugs or chemicals, or particular infections contracted during pregnancy can all cause birth anomalies. Deficiency in folate, alcohol or tobacco use during pregnancy, poorly managed diabetes, and maternal age over 35 years old are all risk factors. It's thought that multiple factors may be needed to cause an anomaly [8]. Congenital anomalies can be detected prenatally via screening tests or diagnosed at birth. Several prenatal tests can identify a variety of abnormalities before delivery [9].

As major birth anomalies have a profound effect on the growing fetus and newborn child; in both industrialized and developing countries and are currently one of the main causes of perinatal mortality [10], therefore, the best course of action is prevention, which is based on knowledge of the potential risk factors, causes of CAs and early prenatal diagnosis. For this goal, appropriate datasets including baseline prevalence of various forms of CA are crucial preconditions for preventative initiatives.

METHODS

Setting and duration

This retrospective study was conducted in a Misurata Neonatal Intensive Care Unit (NICU) from January 2022 to December 2022. The study aimed to examine the occurrence of congenital anomalies in infants admitted to the NICU during this period and analyze the associated mortality rates.

Study Population

The study included all infants with congenital anomalies who were admitted to the NICU during the specified timeframe. A total of 53 infants were included in the analysis.

Data Collection

Data regarding the infants' demographics, gestational age, mode of delivery, presentation, birthweight, and specific congenital anomalies were collected from medical records. Information on maternal factors such as age, parity, and any reported maternal risks or drug usage was also recorded. The study period was divided into monthly intervals to analyze the temporal distribution of admissions.

Data Analysis

Descriptive statistics were used to summarize the collected data. The mortality rate among infants with congenital anomalies was calculated by dividing the number of deaths by the total number of infants in the

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study population. The temporal distribution of admissions was presented using a graphical representation.

Statistical Analysis

Statistical analysis was performed to assess the differences in mortality rates between different groups. The chi-square test or Fisher's exact test was used, depending on the sample size and expected cell frequencies. A p-value less than 0.05 was considered statistically significant.

Ethical considerations

The records were reviewed and data was collected after obtaining relevant ethical approval from Misurata Teaching Hospital's Committee of Scientific Affairs.

RESULTS

A total of 53 infants with congenital anomalies were admitted to the NICU during the study period. The mortality rate was 34% (18 infants). 49% of them (26 cases) were admitted in the last three months of the study period (October to December). The lowest monthly rate of congenital anomalies was reported in May only 2 cases and both survived. (Figure 1) shows the temporal distribution of the admissions with congenital anomalies.

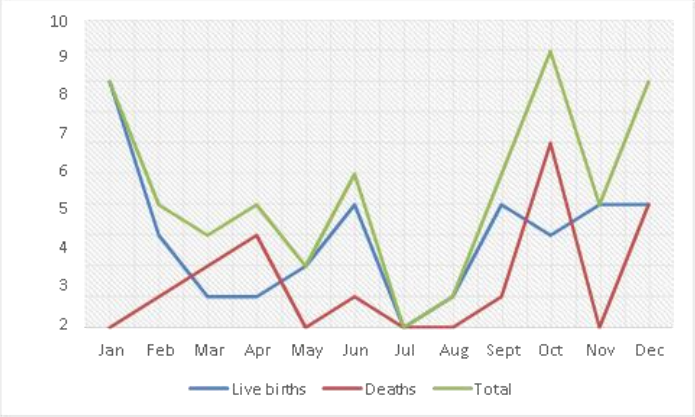

Figure 1. Distribution of admissions and mortalities according to the time of the year

The study involved 30 males (57%) and 23 females (43%). There was no statistically significant difference in mortality between males and females (P = 0.881). The details are shown in (Figure 2).

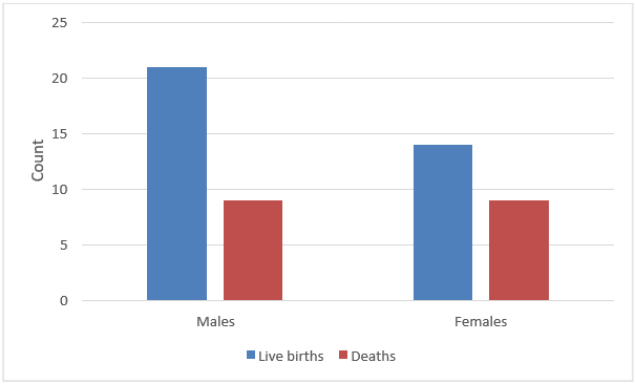

Figure 1. Mortality in both Sexes

The median gestational age was 34 weeks. No live births were recorded before 28 weeks. Most cases were born at 38 weeks 23 cases. The least frequent week was 28 weeks (only 2 cases, both of the survived). The distributions are shown in (Figure 3).

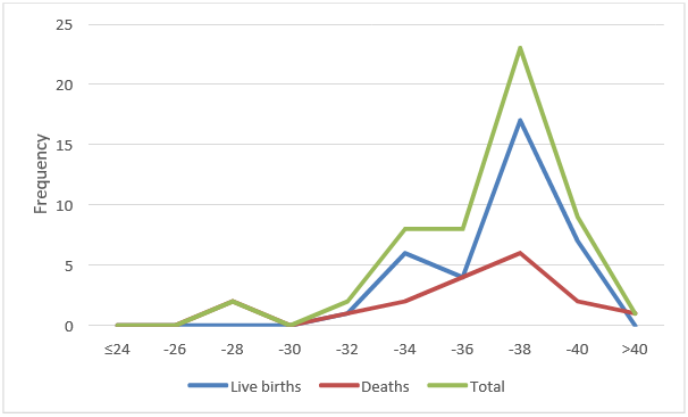

Figure 2. Gestational Age of the Admitted Cases

Most cases were delivered through Cesarian section 37 cases (70%) (Table1). Of those, 18 were elective and 8 were urgent C/S.

Table 1. Delivery Modes of the Admitted Cases

Mode of delivery	Live births	Deaths	Total
NVD	11	5	16
Elective C/S	16	2	18
Urgent C/S	8	11	19

The vast majority of the infants presented cephalically 48 cases (91%), and only 5 cases (9%) were breach presentations. (Figure 3) shows the mortality rates in both presentations.

The median birthweight was '2.5-4' (within the normal birthweight). No cases of extreme birthweights were admitted during the study period. The proportions and percentages of admissions and mortalities by birthweight category are given in (Table 2).

Table 2. Birth Weight Distribution

Birth weight (kg)	Live births	Deaths	Total
>4	5	0	5
>2.5-4	21	8	29
≤2.5 (LBW)	8	5	13
≤1.5 (VLBW)	1	4	5
≤1 (ELBW)	0	1	1

LBW: Low Birth Weight, VLBW: Very Low Birth Weight

Various anomalies were found in the admitted cases (Table 3). Among the anomalies observed, cleft lip & palate had 3 live births, all of which resulted in death. Omphalocele had no recorded live births, but one case ended in death. Edward Syndrome had one live birth without any reported deaths, while Down Syndrome had two live births with no deaths. Potter Syndrome had no live births, but one case resulted in death. Hydrocephalus had three live births, all resulting in death. Genorecurvatum had no recorded live births or deaths. Hypospadias had seven live births without any reported deaths. Undescended testis had two live births, and both cases ended in death. Syndromic baby had one live birth and four deaths.

Table 3. Frequency and Mortality by the Cause of Admission

Congenital Anomaly	Live births	Deaths	Total
Clift lip & palate	3	3	6
Omphalocele	0	1	1
Edward syndrome	1	0	1
Down syndrome	2	0	2
Potter syndrome	0	1	1
Hydrocephalus	3	3	6

Hydronephrosis had no live births but resulted in two deaths. Similarly, anencephaly and encephalocele had no live births but resulted in two and one deaths, respectively. Arthrogryposis had one live birth and one death. Polycystic kidney, meningocele, polydactyly, multiple abdominal mass, imperforated anus, and LL club foot had no live births but resulted in two, one, two, one, one, and one death, respectively. Hydrocele had two live births without any reported deaths. These findings provide valuable insights into the occurrence and outcomes of various anomalies in live births. The causes of admission to the Neonatal Intensive Care Unit (NICU) along with the corresponding number of live births and deaths associated with each cause are sown in (Table 4).

Table 4. Causes of ICU Admission

Cause of admission to the NICU	Live births	Deaths	Total
RDS	7	3	10
Sepsis	4	4	8
TTN	1	0	1
CHD	13	3	16

RDS: Respiratory Distress Syndrome, Transient Tachypnea of the Newborn

Respiratory Distress Syndrome (RDS) led to the admission of 7 live births, with 3 deaths reported among them. Sepsis was responsible for the NICU admission of 4 live births, all of which tragically resulted in death. Transient Tachypnea of the Newborn (TTN) caused the admission of 1 live birth to the NICU, but fortunately, no deaths were reported in this particular case. These findings provide valuable insights into the primary reasons for neonatal NICU admissions and the associated mortality rates. Understanding these causes is crucial for healthcare professionals in providing appropriate care and interventions to improve outcomes for infants requiring specialized neonatal care.

Echocardiography (Echo) was performed on 14 live births, and unfortunately, 3 deaths occurred within this group. Chest X-ray with nasogastric tube (NGT) insertion did not result in any live births or deaths. Ultrasonography (USS) was conducted on 2 live births, and sadly, both cases resulted in death. Computed tomography (CT) scan was performed on no live births, but 1 case resulted in death. Doppler Duplex USS, similarly, had no live births, but 2 cases resulted in death. These findings shed light on the utilization

of various imaging studies in neonatal care and the associated outcomes. The data underscores the importance of appropriate imaging modalities in diagnosing and managing neonatal conditions while acknowledging the potential risks and consequences of these procedures. (Table 5) illustrates the utilization of different imaging studies in the context of neonatal care, along with the number of live births and deaths associated with each study.

Table 5. Imaging Techniques Used on the Patients

Imaging study	Live births	Deaths	Total
Echocardiography	14	3	17
Abdominal USS	2	2	4
CT-Scan	0	1	1
Doppler Duplex USS	0	2	2

Antenatal screening diagnosed 20 cases and none of the remaining cases were diagnosed. The most common diagnosis is polyhydramnios 8 cases (42%). (Table 6) shows all the antenatal diagnoses made in the study cases.

Table 6. Distribution of Antenatal Screening Findings

Antenatal diagnosis	Live births	Deaths	Total
Hydrocephalus	3	4	7
Polyhydramnios	3	5	8
Polycystic kidney	0	1	1
Fetal ascites	0	1	1
Hydronephrosis	0	1	1
Severe oligohydramnios	0	1	1
Encephalocele	0	1	1

Among mothers under the age of 20, there were 5 live births and 1 death. In the age range of 20-29, there were 12 live births and 2 deaths. In the 30-39 age range, there were 8 live births with no reported deaths. Among mothers aged 40 and above, there was 1 live birth and 1 death. The median maternal age, calculated as the midpoint of all recorded ages, is 27 years (Table 7).

Table 7. Maternal Age Distribution

Maternal Age (Years)	Live births	Deaths	Total
≤20	3	1	4
-25	7	2	9
-30	8	3	11
-35	4	14	18
-40	6	3	9
>40	1	3	4

Among women with a parity of "PG", there were 6 live births, 4 deaths were reported. In the parity range of 1 to 5, there were 23 live births, but 12 deaths occurred within this group. For women with a parity of greater than 5, there were 6 live births, and 2 deaths were reported. (Table 8) presents data related to parity, which refers to the number of previous pregnancies a woman has had, along with the corresponding number of live births and deaths.

Table 8. Maternal Parity

Parity	Livebirths	deaths	Total
PG	6	4	10
1--5	23	12	35
>5	6	2	8

Among mothers with diabetes mellitus (DM), there were 3 live births with 1 reported death. In the case of hypertension (HTN), no live births were recorded, but sadly, 2 deaths occurred. Maternal polyhydramnios resulted in 2 live births but tragically led to 5 deaths. Urinary tract infection (UTI) was associated with 1 live birth and 1 death. Maternal antepartum hemorrhage (APH) resulted in 1 live birth with 2 reported deaths. Additionally, maternal oligohydramnios led to 2 (1%) live births accompanied by 2 deaths (1%). (Table 9) displays data regarding maternal risks and their corresponding number of live births and deaths.

Table 9. Prenatal Complications

Maternal risks	Livebirths	Deaths	Total
DM	3	1	4
HTN	0	2	2
Polyhydramnious	2	5	7
UTI	1	1	2
APH	1	2	3
Oligohydramnios	2	2	4

DM: Diabetes Mellitus, HTN: Hypertension, UTI: Urinary Tract Infection, APH: Ante-Partum Hemorrhage

Among mothers who were prescribed insulin, there were 2 live births (1%), and no deaths were reported. Similarly, for mothers using oral hypoglycemic medications, there was 1 live birth, and no deaths occurred. In contrast, the mothers using of antihypertensive had no live births but sadly led to 2 deaths (1%). Maternal usage of thyroxine was not reported in the records. (Table 10) presents data on

maternal drug usage and the corresponding number of live births and deaths.

Table 10 Drugs Used by the mothers

Maternal drugs	Livebirths	Deaths	Total
Insulin	2	0	2
Oral hypoglycemic	1	0	1
Antihypertensive	0	2	2

DISSCUSION

Congenital anomalies (CAs) are a major contributor of morbidity and mortality in early life. In our study, we aimed to assess the incidence, risk factors, and outcomes of major CAs in Misurata Hospital.

The mortality rate among infant with CA in our study was 34% (18 infants out of 53). In our previous published study, in 2015, the mortality rate was significantly lower (29%) [11]. A similar rate of 36.7% and 33.4 was seen in a study in Malta [12] in 2014, and recent 10-years-retrospective study in Ghana [13], while a significantly lower rates of 10.4%, 15.4%, were seen among other studies [14-15].

There was a higher number of males, but there wasn't a significant association could between male sex and death. Male predominance was also seen in our previous study [11], and most other studies [15-17]. In 2014, a national population-based study suggested a 26% higher risk for males to develop CA [18]. This could be explained as the female sex was found to be associated with more fatal congenital anomalies and were unable to live to be born with signs of life, it was assumed that there were more male babies with birth defects19, and female being a protective factor [17].

Despite the strong stated association between prematurity and CA, which was also seen in our previous study [11] beside others [17], no significant relation could be made in this study as most cases were born at 38 weeks. Gestational age was not seen to be associated with CAs in a study by Ajao et al in Nigeria [14].

Cesarean section was associated with 2.6 times higher chance of congenital anomalies death than mothers who had a normal delivery, which is consistent with our previous study [11] and also other recent researches [15,20-21]. Nevertheless, these findings contraindicated those of other researches, which linked the improper positioning of the fetus in the uterus during the cesarean operation [22-23]. As many CA are detected by prenatal tests, therefore this discrepancy may be explained by the vaginal route's potential to damage brain tissue and expose it to microorganisms that are often found in the birth canal so C/S is one of the prophylactic measurements [24].

As our previous study [11], cephalic presentation is still the major type of presentation at time of delivery. Although other papers have linked breech presentation to higher rates of anomalies especially among full term babies [25].

There was no association between birth weight and the presence of congenital anomaly, in contrary, normal birth weights had higher rates for CA but infant with LBW is more likely to die. This is consistent with our previous study [11], and other studies from Uganda [26], however it disagrees with most other studies where strong association was documented [15,20,27].

CHD, Hypospadias, cleft lip and palate, hydrocephalus, and Syndromic baby were the most prevalent anomalies seen with 30.2%, 13.2%, 11.3%, 11.3%, and 9.43% respectively. This is consistent with the studies stating that CHD are globally the most common severe birth defects [28]. Although with lower rates, CHD were the also the most prevalent anomalies among newborns in other studies [29-30] but with different order for the rest of anomalies. Other papers found nervous system anomalies to the most prevalent [16]. The discrepancy may be due to sociodemographic variations. Among all anomalies, Syndromic baby was the most anomaly among mortality rates. This correlates with our previous study [11].

Major mortality rates were seen among newborns admitted to NICU due to sepsis. In this study, major anomaly was the leading type of anomalies and these children are known to be more susceptible to sepsis according to other papers [31]. More understanding of this relationship is needed for healthcare professionals

in providing appropriate care and interventions to improve outcomes for infants requiring specialized neonatal care.

Maternal age has always been an important risk factor regarding congenital anomalies [32]. This is also seen in this present and our previous study [11]. Maternal age >35 years have been linked to higher rates of congenital anomalies and higher mortality rates. Many other studies have also stated this association such as Singh et al., (2000) in Libya [27], Refat et al., in UAE [33], and Zolfizadeh et al., in Iran [20]. Other studies suggest this relation to both ends of extreme age, i.e. younger than 20 years and older than 35 years old [17]. In the other hand, few other studies did not find a significant relation [34].

Multiple parity has been associated with increased rates of congenital anomalies. This finding is consistent with our result and the result of our previous study as well. This was a well-established risk factor also among other studies too [15,27], while some other research has shown a correlation between nulliparity and a higher risk of a wide range of birth abnormalities [35]. Inconsistencies in the literature on parity and CA may be explained by unmeasured confounding because many of the earlier research only looked at a small number of confounding factors [36]. In other words, prior research did not account for fetal loss history, gestational hypertension, or infertility in the mother as there is evidence linking each of these variables to certain kinds of birth abnormalities. Duong HT et al (2015) established a case control study to look if parity was an independent risk factor for CA. The study stated that the odds of having infants with amniotic band sequence, hydrocephaly, esophageal atresia, hypospadias, limb reduction deficiencies, diaphragmatic hernia, omphalocele, gastroschisis, tetralogy of Fallot, and septal cardiac defects were significantly higher (1.2 to 2.3) in nulliparous mothers compared to primiparous mothers, while multiparous mothers had a significantly lower incidence of hypospadias and limb reduction deficits but a significantly higher risk of omphalocele as compared to primiparous mothers [36].

In our study, the most prevalent prenatal and maternal risk factors are polyhydramnios followed by DM and oligohydramnios. It is well-known that a higher risk of several fetal congenital abnormalities is linked to polyhydramnios [37]. The European Surveillance of Congenital Anomalies stated that the incidence of fetal abnormalities associated with polyhydramnios was roughly ten times greater than the general prevalence of fetal congenital anomalies in Europe [39]. Also, there is a correlation between pregestational maternal diabetes and an elevated risk of overall CA. Studies show that maternal diabetes raises the chance of abnormalities by two folds. Diabetes-related abnormalities typically affect one or more organs, while mainly causing CHD, musculoskeletal and central nervous system anomalies. Although the precise mechanism remains unknown, hyperglycemia is believed to be the main teratogen responsible for heart abnormalities which are the most prevalent CA in our study [38].

Due to the small study population, no significant relation could be built regarding maternal drugs and CA. There is an ongoing debate regarding the association of hypoglycemic drugs and CAs. Many studies suggest that individual patient risk seems to be associated more with maternal glycemic control than with the type of antidiabetic medication used in the first trimester of pregnancy [39]. Most hypoglycemic drugs are safe to be used during pregnancy for mild and hyperglycemia, however there are no data on the long- term health effects of the offspring's exposure to metformin or glyburide since the safety features of these oral hypoglycemic medications are restricted to the prenatal stage [40].

In addition to an increased risk of miscarriage and stillbirth, the use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers during pregnancy has been linked to cardiovascular, central nervous system, and urinary tract abnormalities. Overall, less than 1% of congenital abnormalities in

the general population are caused by drug exposure [41].

Limitations

The study was retrospective in nature, relying on data collected from medical records, which may have contained missing or incomplete information. The study was conducted in a specific NICU, limiting the generalizability of the findings to other settings. Additionally, the study period and sample size were relatively small, potentially impacting the statistical power and generalizability of the results.

CONCLUSION

Congenital anomalies among infants are linked to neonatal mortality and morbidities. The prevalence of congenital anomalies among NICU admissions. They also contribute to the mortality, short- and long-term morbidity, and they can be linked to antenatal factors and maternal health as well. Congenital anomalies pose a substantial burden on neonatal health in this setting. Cesarean section, sepsis, and specific maternal factors were identified as risk factors. These findings underscore the importance of tailored care for mothers and infants with congenital anomalies to improve outcomes.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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