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ORIGINAL ARTICLE

# Frequency of congenital anomalies in a Neonatal Intensive Care Unit in Brazil

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**Keywords:**
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## Abstract

**Objectives:** To evaluate the rate of congenital anomalies in newborns who were admitted in a Neonatal Intensive Care Unit. **Methods:** Evaluation of hospitalized patients' medical records between January/2012 and December/2015 in Neonatal Intensive Care Unit from Western Paraná University Hospital, in Cascavel City - State of Paraná. Evaluated variables were: sex, maternal age, gestational age, birth weight, index of Apgar, a correct prenatal care, maternal diseases, gestational intercurrences, consanguinity and outcome. The mothers were grouped on three age groups: mothers up to 18 years old, mothers between 19 and 34 years old and mothers above 35 years old. The statistical analyze was performed by software R Core Team using the RStudio platform, sharing in descriptive statistics: absolutes frequencies - n, and relatives percent frequencies - %. To frequencies of the variables' categories were used Chi-square test of proportions comparison and Chi-square test of adhesion, using level of significance to $p < 0.05$. **Results:** A total of 888 newborns were hospitalized in the Neonatal ICU, being some type of anomaly was detected in 127 (14.3%). The most common malformations during period of evaluation were: Congenital heart disease (19; 15%), hydrocephalus (16; 12.6%) and gastroschisis (14; 11%). Regarding the newborns' evolution during period that they were hospitalized, 48.8% were discharged from the hospital, 39.4% died and 11.8% were referral to another services. **Conclusion:** The rate of congenital anomalies was 14.3%, with high mortality rate. The most common malformations were in the cardiovascular system, central nervous system and gastrointestinal tract.

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## INTRODUCTION

A congenital anomaly can be defined as structural or functional defects that are present from birth[1]. Structural defects represent an innate error in morphogenesis and may developed from four categories of developmental pathogenesis: malformation, i.e., inadequate tissue formation; the deformation due to intrinsic forces; disaggregation resulting from damage to previously normal tissue; and dysplasia with cell disorganization within the tissues[2].

Congenital malformations are defined as greater when they bring clinical or aesthetic consequences to the patient, they can frequently occur with high morbimortality, and leave important functional sequelae; and minor congenital malformations are those that do not cause significant problems to the patient. When there are three or more minor anomalies, approximately 19.6% to 26% of the patients may present with larger malformations and should be evaluated[2].

Heart diseases are the most common anomalies in newborns and the most frequent cause of infant death due to congenital defects[3]. Neural tube defect is the most frequent congenital malformation of the central nervous system, a recent interventional study showed that about 90% of neural tube defects and 40% of congenital heart defects can be avoided with periconceptional folic acid intake (at least one month before conception and at least two months after conception)[4].

In order to reduce morbidity and mortality rates in the neonatal period, it is necessary to know the regional characteristics of each service, such as the frequency of congenital malformations, the identification of the associated risk factors, and to value early diagnosis, primary and secondary prevention.

The goal of this study was to determine the rate of congenital anomalies detection in neonates admitted to a neonatal intensive care unit (ICU) and to associate them with the perinatal epidemiological profile.

## METHOD

We performed a retrospective analysis of medical charts of newborns admitted between January 2012 and December 2015 to the neonatal ICU of the Oeste do Paraná University Hospital (HUOP), in the city of Cascavel - Paraná. Congenital anomalies were identified through a physical examination description, laboratory workup and imaging reports. The variables analyzed were gender, maternal age, type of delivery, gestational age by the Capurro method, birth weight, Apgar score, smoking, proper prenatal care (≥ 6 visits), maternal gestational diseases, consanguinity, outcome (hospital discharge, transfer to another service or death). Maternal age was stratified in ≤ 18 years; between 19 and 34 years; ≥ 35 years. Multiple malformations was the term used for patients with three or more minor congenital anomalies. We grouped the anomalies by systems to analyze the frequency over the years. To study the most prevalent variables and frequency throughout the period, we analyzed the anomalies individually. As for exclusion criterion, we selected those newborns with up to two minor congenital malformations.

For the statistical analysis, we used the R (R Core Team, 2016) software - RStudio (RStudio Team, 2015) platform. The questions were made out of descriptive statistics (absolute frequencies: n and relative percent frequencies:%). The frequencies of the variables' categories were analyzed using the Chi-Square test to compare proportions and the chi-square test for compliance. For statistical significance we used $p$ <0.05.

The Research Ethics Committee of the Oeste do Paraná State University under protocol number 1.545.279/2016 approved this study.

## RESULTS

During the evaluation period we assessed 888 newborns admitted to the neonatal ICU and 127 (14.3%) presented congenital anomalies. Although eight patients (6.2%) presented more than one malformation, for analysis purposes we decided to consider the anomalies individually.

There was no difference in detection frequency during the study period. The majority of the deliveries happened by C-section (70.1%) and had adequate prenatal care (76.4%). Fourteen mothers had psychiatric disorders, gestational-specific hypertensive disease, diabetes mellitus, premature placental detachment, toxoplasmosis; 104 were non-smokers (81.9%) and one of the pregnant women presented consanguinity (0.8%). As for the evolution of newborns during hospitalization, 62 (48.8%) were discharged, 50 (39.4%) died and 15 (11.8%) were transferred to referral services (Table 1).

### Characterization of congenital anomalies

The most prevalent anomalies of the evaluation period (2012 to 2015) was congenital heart disease (19; 15%), hydrocephalus (16; 12.6%), gastroschisis (14; 11%), multiple malformations (14; 11%), esophagus atresia (12, 9.4%), myelomeningocele (11; 8.6%) and imperforate anus (9.7%). The remaining 32 (25.2%), less prevalent, are presented in Table 2.

**Table 1.** Absolute (n) and percent-relative frequencies (%) of the variables associated with the general sample characterization.

| Variable | IR | n | % | *p* Value |
|---|---|---|---|---|
| Birth Year | 2012 | 36 | 28.3 | 0.839 |
| | 2013 | 31 | 24.4 | |
| | 2014 | 29 | | |
| | 2015 | 31 | 24.4 | |
| Gender | Female | 58 | 45.7 | 0.421 |
| | Male | 67 | 52.8 | |
| | NIR* | 2 | 1.6 | |
| Delivery | Vaginal | 29 | 22.8 | < 0.001 |
| | C-Section | 89 | 70.1 | |
| | NIR* | 9 | 7.1 | |
| Proper Prenatal Care | Yes | 97 | 76.4 | < 0.001 |
| | No | 17 | 13.4 | |
| | NIR* | 13 | 10.2 | |
| Smoking | Yes | 11 | 8.7 | <0.001 |
| | No | 104 | 81.9 | |
| | NIR* | 12 | 9.4 | |
| Outcome | Hospital Discharge | 62 | 48.8 | <0.001 |
| | Death | 50 | 39.4 | |
| | Transfer to another clinic | 15 | 11.8 | |

*NIR - Not in the records.

### List of anomalies with year of birth

Table 3 shows the categories of abnormalities in the years 2012 to 2015, it is noteworthy that in 2012, 2013 and 2014, gastrointestinal malformations were more frequent (47.05%, 53.33% and 44.44%, respectively) and in the year 2015 cardiovascular malformations prevailed (36.66%).

### Association between anomalies and maternal age

Table 4 presents the categories of abnormalities for mothers at different age groups. We noticed that gastrointestinal malformations were the most frequent of all, being 56.25% for mothers up to 18 years of age; 39.47% for mothers aged 19 to 34 years and 42.85% for mothers over the age of 35 years.

When comparing the frequency of abnormalities with maternal age, we found a significant difference for anencephaly ($p$ = 0.02) and gastroschisis ($p$ > 0.001) in mothers up to 18 years of age; and Down syndrome ($p$ = 0.001) for mothers over 35 years of age (table 4).

## DISCUSSION

The prevalence of newborns with congenital anomalies in the neonatal ICU (14.3%) was similar to that found

**Table 2.** Relative frequencies (%) of the anomalies according to maternal age stratification.

| Malformation | < 18 | 19-34 | > 35 | *p* value |
|---|---|---|---|---|
| Corpus callosum agenesis | 0 | 1.4 | 0 | 0.7 |
| Genital and anal agenesis | 0 | 1.4 | 0 | 0.7 |
| Karyotype changes | 0 | 1.4 | 0 | 0.7 |
| Anencephaly | 12.5 | 1.4 | 0 | 0.02* |
| Congenital multiple arthrogryposis | 4.1 | 0 | 0 | 0.14 |
| Esophagus atresia | 12.5 | 5.7 | 13 | 0.4 |
| Duodenal atresia | 4.1 | 4.2 | 8.6 | 0.68 |
| Complex heart disease | 0 | 1.4 | 0 | 0.7 |
| Congenital heart disease | 0 | 15.7 | 21.7 | 0.07 |
| Frontal lobe cystic encephalopathy | 0 | 1.4 | 0 | 0.71 |
| Ureteropyelic junction encephalopathy | 0 | 1.4 | 0 | 0.71 |
| Ureteropyelic junction stenosis | 0 | 1.4 | 0 | 0.71 |
| Syndromic face | 0 | 1.4 | 4.3 | 0.5 |
| Labiopalatine cleft | 4.1 | 0 | 0 | 0.14 |
| Complete bilateral transforaminal fissure | 4.1 | 0 | 0 | 0.14 |
| Rectovesical fistula | 0 | 1.4 | 0 | 0.7 |
| Tracheoesophageal fistula | 0 | 2.8 | 0 | 0.5 |
| Gastroschisis | 33 | 7.1 | 0 | < 0.001* |
| Diaphragmatic hernia | 0 | 2.8 | 4.3 | 0.62 |
| Hydrocephaly | 12.5 | 17.1 | 0 | 0.1 |
| Hydronephrosis | 0 | 1.4 | 0 | 0.7 |
| Fetal hydrops | 4.1 | 1.4 | 0 | 0.52 |
| Pulmonary hypoplasia | 0 | 1.4 | 0 | 0.7 |
| Anal imperforation | 4.1 | 5.7 | 4.3 | 0.94 |
| Macrocephaly | 0 | 0 | 4.3 | 0.12 |
| Anorectal malformation | 0 | 1.4 | 0 | 0.7 |
| Cystic pulmonary adenomatous malformation | 0 | 1.4 | 0 | 0.7 |
| Congenital megacolon | 8.3 | 1.4 | 8.7 | 0.17 |
| Single lower limb | 0 | 1.4 | 0 | 0.7 |
| Meningomyelocele | 4.1 | 12.8 | 0 | 0.11 |
| Multiple malformation | 4.1 | 14.3 | 13 | 0.4 |
| Omphalocele | 4.1 | 2.8 | 4.3 | 0.91 |
| Polycystic kidney | 0 | 1.4 | 0 | 0.7 |
| Aicardi syndrome | 0 | 0 | 4.3 | 0.12 |
| Down syndrome | 4.1 | 0 | 17.4 | 0.001* |
| Edwards syndrome | 0 | 1.4 | 8.7 | 0.10 |
| Vitelline sac tumor | 0 | 1.4 | 0 | 0.7 |
| Congenital volvulus | 0 | 1.4 | 0 | 0.7 |

*Statistically significant values.

**Table 3.** Absolute (n) and percent-relative frequencies (%) of the anomalies' categories stratified by larger frequency systems during the years of the study.

| Year | Malformations | n | % | *p* Value |
|---|---|---|---|---|
| 2012 (n = 35) | Cardiovascular | 9 | 26.47 | < 0.0001 |
| | Gastrointestinal | 16 | 47.05 | |
| | Genitourinary | 1 | 2.94 | |
| | Neurological | 7 | 20.58 | |
| | Thoracic | 1 | 2.94 | |
| 2013 (n = 30) | Cardiovascular | 3 | 10 | < 0.0001 |
| | Gastrointestinal | 16 | 53.33 | |
| | Neurological | 6 | 20 | |
| | Thoracic | 1 | 3.33 | |
| | Skeletal | 4 | 13.33 | |
| 2014 (n = 27) | Cardiovascular | 1 | 3.7 | < 0.0001 |
| | Gastrointestinal | 12 | 44.44 | |
| | Genitourinary | 1 | 3.70 | |
| | Neurological | 9 | 33.33 | |
| | Thoracic | 1 | 3.70 | |
| | Skeletal | 6 | 22.22 | |
| 2015 (n = 30) | Cardiovascular | 11 | 36.66 | 0.003 |
| | Gastrointestinal | 9 | 30 | |
| | Neurological | 9 | 30 | |
| | Thoracic | 2 | 6.66 | |
| | Skeletal | 3 | 10 | |

in a study carried out in Turkey, where the prevalence was 13.7%[5]. In comparison, the European Surveillance of Congenital Anomalies (EUROCAT) recorded a total prevalence of congenital anomalies of 2% between 2003 and 2012[6,7], and in a study carried out in the United States of America from 2011 to 2013, the prevalence was found to be 3%[8], however, both studies are population-based, which justifies the higher frequency found in this study with neonates hospitalized in an ICU that is a reference center for high-risk pregnancies.

Congenital heart diseases are the most common malformations present at birth in newborns, and an important cause of infant death[5,9,10], as evidenced in this study, where the most prevalent malformations during the period evaluated (2012 to 2015) were congenital heart diseases. Differently from what was shown in a study in Taiwan, where congenital kidney and urinary tract abnormalities were found in 0.42 per 1,000 births within the general population[11]. In this study, carried out in the ICU, there was a prevalence of 3%, and the difference can be justified by the evaluations performed in different risk groups. In Germany, kidney and urinary tract congenital anomalies represent 1.6%, and in Brazil, they correspond to 2.9% of the cases[12].

**Table 4.** Absolute (n) and percent-relative frequencies (%) of the anomalies' categories stratified by larger frequency systems considering the maternal age ranges.

| Age | Malformations | n | % | *p* Value |
|---|---|---|---|---|
| ≤ 18 years (n = 16) | Cardiovascular | 1 | 6.25 | < 0.0001 |
| | Gastrointestinal | 9 | 56.25 | |
| | Neurological | 7 | 43.75 | |
| | Skeletal | 2 | 12.5 | |
| Between 19 and 34 years (n = 76) | Cardiovascular | 15 | 19.73 | < 0.0001 |
| | Gastrointestinal | 30 | 39.47 | |
| | Genitourinary | 1 | 1.31 | |
| | Neurological | 22 | 28.94 | |
| | Thoracic | 4 | 5.26 | |
| | Skeletal | 10 | 13.15 | |
| Older than 35 years (n = 21) | Cardiovascular | 5 | 23.81 | 0.011 |
| | Gastrointestinal | 9 | 42.85 | |
| | Genitourinary | 1 | 4.76 | |
| | Neurological | 2 | 9.52 | |
| | Thoracic | 1 | 4.76 | |
| | Skeletal | 2 | 9.52 | |

In Kuwait, one study found central nervous system malformation as more prevalent, followed by cardiovascular, skeletal and gastrointestinal malformations[13]; whereas in this study the prevalence of cardiovascular malformations was higher than those in the central nervous system, followed by gastrointestinal malformations.

Maternal age is a risk factor for abnormal intrauterine fetal development; advanced maternal age (≥ 35 years) may be associated with an increased risk for Down syndrome[15-16] and chromosomal abnormalities[10], as in this study, this association also proved to be true.

Congenital anomalies have a multifactorial etiology, besides the genetic factor, the environmental factor related to exposure to smoking may be associated[17]. The risk of anomalies increases with exposure; the greater the number of cigarettes smoked per day, the greater the risk[17,18]. In the present study, there was a prevalence of 8.7% (11) of smokers; the number of women who were passively exposed to tobacco during gestation was not raised.

As for the evolution of newborns during hospitalization, 39.4% died an outcome that was higher than that estimated by the WHO in 2004, where about 7% of the neonatal deaths in the world were caused by congenital anomalies[1]. This study was also compared to the study carried out in the USA (2011-2013), where infant mortality was attributed due to an underlying cause of congenital anomalies in 20%[8].

Similar results were found in Japan (2007 to 2011) and in Chile (1997 to 2011), with neonatal deaths attributed to congenital malformations in 29.4% and 35.8% of the cases, respectively[19,20]. According to Brazilian data from 2014, congenital malformations represented 22.8% of the neonatal death causes, and only prematurity was more frequent (33.3%)[21]. This mortality rate, considered high in the present study, may be related to uninvestigated causes, such as prematurity and infection.

A Japanese study reported that more than half of the congenital anomalies (59%) were diagnosed in the prenatal period[20]. Adequate prenatal screening is important and essential; the first trimester screening method is effective in detecting important fetal structural abnormalities in low-risk pregnancies, and it is indicated during the 12th to 13th weeks and six days of gestation, thus diagnosing about 40.6% of the cases[22]; other authors have already argued that the ideal time for the investigation is from the 18th to 20th weeks for better visibility of the fetal anatomy[23].

Obstetric care is of great importance during prenatal care, especially congenital anomalies associated with vitamin deficiencies. In this study, a significant difference of anencephaly and gastroschisis in young mothers (≤ 18 years) was found when compared to other anomalies. Such relationship is associated with studies that show that adolescent mothers generally belong to low socioeconomic groups, are less educated, are single and less prone to adequate prenatal care[10]. The use of folic acid during prenatal care is recommended to avoid anencephaly (neural tube malformation)[4]. Therefore, the morbidity and mortality rates of newborns with severe birth defects could be reduced with measures that promote adequate prenatal care and early diagnosis.

Epidemiological studies on congenital anomalies are limited because they require the analysis of large populations with well-organized and comparable diagnoses. The veracity of registers and encodings vary according to location and time[24]. Thus, the medical records were a limitation in this study, because it presented incomplete information about many patients. In conclusion, the rate of congenital anomalies detection in this study was 14.3%. Changes in gastrointestinal tract, cardiovascular and central nervous system were the most frequent.

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