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ORIGINAL ARTICLE

Congenital Malformations in the Newborn Population: A Population Study and Analysis of the Effect of Sex and Prematurity

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Background: Congenital malformation (CM) is a leading cause of infant mortality. We hypothesized that the current estimates of the prevalence of CM are obsolete because of the increased rate of terminating fetuses with severe CMs and the widespread use of prenatal vitamins.
Methods: This population-based cross-sectional study analyzed the effect of sex and prematurity on CM prevalence. All data were derived from birth entries in the 2008 Nationwide Inpatient Sample (NIS) database. Our objectives were to determine the prevalence of CM diagnoses among all birth hospitalizations in 2008 and to analyze the effect of sex and gestational maturity on CM prevalence.
Results: We identified 29,312 patients with CMs from among 1,014,261 live births, which yielded a CM prevalence of 28.9 per 1000 live births. Associated genetic syndromes were present in 1172 (4%) patients. Among newborns with nonsyndromic CM, 91% of newborns had an isolated CM and 9% of newborns had multiple CMs. The cardiovascular system was the most commonly involved organ system. The risk of CM was significantly higher in preterm newborns for an isolated CM [odds ratio (OR), 1.5; confidence interval (CI), 1.4—1.5]; multiple CMs (OR, 2.1; CI, 2.0—2.3); and overall CMs (OR, 1.4; CI, 1.3—1.5). Males had higher risk of isolated CMs (OR, 1.3; CI, 1.2—1.5). However, there was no sex difference in the risk of overall CM.
Conclusion: We reported up-to-date national estimates of the prevalence of CM, which is important for monitoring trends, determining service planning, and assessing disease burden because of congenital malformations in the United States of America. We also showed a strong association between CM and prematurity. Further study of this association is needed to provide insight into the etiology of these relatively common public health problems.

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1. Introduction

A congenital malformation (CM) or birth defect is defined as a structural or chromosomal malformation with a significant impact on the health and development of a child.[1] It contributes significantly to infant mortality and morbidity. Over the years, the proportion of infant mortality due to CM has increased significantly from 15.1% in the 1970s to 22.1% in the late 1990s, which makes it the leading cause of infant mortality.[2,3] With regard to morbidity, congenital malformations account for 12% of all pediatric hospitalizations. This subset of patients with CMs has longer hospital stays and incurs higher hospitalization costs, compared to other patients.[4] In the United States population, an estimated 2.3% of cases of premature death and disability, as measured by disability-adjusted life years, occurs because of congenital abnormalities.[5] Based on these findings, it is apparent that CM is a major public health problem because of its significant contribution to mortality and morbidity.

Studies published worldwide report a birth prevalence of CM that ranges 20—55 per 1000 live births with significant variation, depending on the demographics of the study population, the study design, and the method of case ascertainment.[1,6—10] Most prevalence rates are estimates derived from clinical studies of small sample populations or population-based studies from a specific geographic location. Considering the heterogeneity of the Unites States population, estimates from these studies may not be representative of the true CM prevalence in the nation. In addition, there is a significant variation in the inclusion criteria or in the definition of CM in these different studies, which makes it difficult to compare data from these different studies.

There has been a tremendous progress in the prenatal diagnosis of CM because of improvements in fetal ultrasound and prenatal genetic testing. This allows parents the choice of terminating the pregnancy. In the past 2 decades, there has also been a concordant increase in the rate of termination of pregnancy for fetal anomaly.[10,11] Some studies have shown that prenatal folic acid and other multivitamin supplementation significantly decrease the birth prevalence of some CMs.[6—8] We hypothesized that these factors altered the birth prevalence of CM, which rendered estimates from older studies obsolete. The purpose of our study was therefore to provide up-to-date estimates of the current CM prevalence in the United States.

2. Materials and methods

All data were derived from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP) by the Agency for Healthcare Research and Quality (Rockville, MD, USA).[12] The 2008 NIS is an all-payer administrative database that reports clinical and resource use information that is representative of hospitalizations in 42 states. We chose the NIS database instead of other databases such as the Kids' Inpatient Database (KID) because the NIS is the largest available inpatient care database in the United States. It contains approximately 8 million hospital stays each year from approximately 1000 hospitals that were sampled to approximately 20% stratified sample of community hospitals in the United States. The large sample size of the NIS makes it ideal for analyzing rare conditions such as specific CMs. In addition, most newborn deliveries occur in adult hospitals and the NIS captures these hospitalizations; hence, this provided an invaluable resource for achieving our primary objective of estimating the birth prevalence of CMs. We chose the 2008 dataset because it was the latest available NIS dataset at the inception of this study. Approval for this study was obtained from HCUP and from the Institutional Review Board (New York, USA).

We reviewed the NIS database from January 2008 to December 2008 and identified 1,204,887 live births (i.e., birth hospitalizations). We included 1,014,261 (84%) live births with available sex and gestational age data in our final cohort. All cases of CM diagnoses during birth hospitalization were identified by ICD9 code 740.0—759. These diagnoses were made clinically or by autopsy of infants of live births that died during birth hospitalization. To avoid double counting, we restricted our inclusion criteria to CMs diagnosed during birth hospitalization. We ensured this by including only hospitalizations with ICD-9 code for normal and complicated delivery (650.0—669.0); hence, this excluded diagnoses made during interhospital transfer or during readmission hospitalization.

In patients with multiple CMs, each malformation was counted separately. We grouped all CMs by different organ systems. Based on the classification system by Christensen et al,[13] we defined multiple organ system involvement as live births with CMs that involved two or more organ systems. For gestational maturity, the NIS coding system defined preterm birth and term birth as delivery before and after 37 completed weeks of gestation, respectively. We analyzed 62 selected CM diagnoses to determine the effect of sex and gestational maturity on the birth prevalence of CM. For the odds ratio calculation, we considered males as the exposed group for sex, and preterm births as the exposed group for gestational maturity. We excluded genitourinary malformations from our sex analysis because of differences between the sexes in the spectrum of genital malformations.

Data weighting was performed with SAS software (NC, USA) in accordance with the HCUP recommendations.[14] The NIS has undergone some changes over time in sampling strategy, weighting strategy, and data element available. We adjusted for these changes in accordance with the recommendations in the NIS Trend Supplemental files available at http://www.hcup-us.ahrq.gov/db/nation/nis/nistrends.jsp.[15] This analysis excluded CM diagnoses with a cell size of 10 or fewer in keeping with the HCUP data use agreement, which prohibits reporting cell sizes of 10 or fewer. The CM prevalence was expressed per 1000 live births and then stratified by sex and gestational maturity. We used the Chi-square test to assess differences between groups. A p value of <0.05 was considered statistically significant. We then used MedCalc for Windows, version 12.5 software (MedCalc Software, Ostend, Belgium) to estimate the odds ratio (OR) and the 95% confidence interval (CI) to assess the effect of sex and prematurity on CM prevalence.