Brief Report

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Prevalence and maternal-child clinical and socioeconomic factors associated with congenital anomalies in a Mexican hospital-based setting

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SUMMARY: There is controversial evidence that some selected congenital anomalies (CA) are associated with sex, maternal age, urban-rural residence, or socioeconomic status among the Hispanic population. This study aimed to assess the prevalence and maternal-child clinical and socioeconomic factors across a wide range of CA in a hospital-based setting from northwest Mexico. From January to December 2023, a cross-sectional study for CA and live births at Durango General Hospital was performed. Hospital-based prevalence was calculated for all CA subtypes and grouped anatomical system defects. Associations with CA and subgroup analysis were conducted to assess newborn sex, maternal age, residence, and socioeconomic factors on CA prevalence, using Pearson's chi-squared test and Fisher's exact test. Probability of CA was estimated based on logistic regression analysis along with odds ratio (OR) and its 95% confidence interval. All tests were two-sided with p values < 0.05 considered statistically significant. A total of 6,784 newborns and 306 CA were assessed (hospital-based prevalence 4.5%). Males, maternal age < 20 and ≥ 35 years, urban residence, and lowest socioeconomic status were associated with CA (all OR > 1.0 and p < 0.05). Subgroup analysis indicated associations between males and cardiovascular and genitourinary defects; maternal age < 20 years and craniofacial and abdominal defects; maternal age ≥ 35 years and digestive and chromosomal abnormalities; mother's urban residence and craniofacial, cardiovascular, genitourinary, and abdominal defects; socioeconomic levels D-E and craniofacial and cardiovascular defects (all OR > 1.0 and p < 0.05). These findings reflect noticeable components associated with several CA and might be relevant for prevention and maternal-child health.

Keywords: congenital abnormalities, maternal age, Mexico, socioeconomic status, prevalence

1. Introduction

Congenital anomalies (CA) are structural abnormalities that encompass a broad array of phenotypes with an accepted prevalence of 3%, causing 240,000 neonate deaths each year (*1*), and imposing a considerable cost of care on societies and healthcare systems (*2*). Around one in three cases of CA can be attributed to a known cause and thought to result from complex gene-environment interactions (*3*), whereas evidence on the association of CA with common epidemiological features seems limited (*4*). Overall, CA may be more common in males (*5*), young and advanced maternal ages (*6*), urban residence (*7*), and adverse socioeconomic conditions (*8*). In contrast, other studies have shown a decreased effect of advanced maternal age or sex differences according to specific CA (*9,10*). Thus, the above discussion shows that risk factors for CA vary considerably across studies.

Moreover, race and ethnicity as social constructs may depend on socioeconomic features and are known to be substantial contributors to healthcare disparities (*11*). In this sense, Mexican patients may have particular epidemiological and socioeconomic characteristics derived from limited-resource settings, bypassing preventive healthcare which could be related to CA (*12,13*). Therefore, understanding differences in these factors can also provide clues about plausible social and biological mechanisms that may influence the occurrence of CA in vulnerable populations.

To date, population-based studies addressing clinical and socioeconomic factors in CA among the Hispanic race remain controversial and have been

limited to analyzing its influence on selected CA (*14-19*). Furthermore, no study has estimated the aforementioned influences across a wide range of CA in Mexico, hence preventing the recognition of clinical and socioeconomic-related factors and their differences from other populations. To contribute to the aforementioned, this study aimed to assess the prevalence and maternal-child clinical and socioeconomic factors associated with CA in a Mexican hospital-based setting.

2. Materials and Methods

2.1. Study design and ethics statement

A cross-sectional study was conducted on data of mother-child pairs from January to December 2023 at Durango General Hospital. The latter is a regional center for maternal and child care for low-income population attending to 25% annual births of Durango state in northwest Mexico. Newborns with birth weight > 500 g or gestational age > 20 weeks whose parents were Mexican mestizo origin were included. Informed consent was obtained from all participants for epidemiological and research purposes (*3*). Major exclusion criteria included stillbirths, records of participants residing outside Durango state, and missing data for covariates of interest. Approval for human participants research was obtained from the Ethics Committee of Durango Secretary of Health (number 007/2023). The study was conducted under the Declaration of Helsinki and was strictly voluntary, confidential, and safe. Strengthening the reporting of observational studies in epidemiology guidelines were followed.

2.2. Data collection and study variables

Using a standardized form, data were collected through the hospital-based birth defect surveillance program by experienced doctors and the principal investigator supervised the process daily to conduct comprehensive quality control (*3*). Cases were identified as those with at least one major CA and were evaluated by a clinical geneticist, who performed a thoughtful clinical dysmorphology examination of all potential cases and also interviewed at least one parent to collect and verify background data.

According to the World Health Organization International Classification of Diseases (tenth revision) (*20*), CA were classified into 20 subtypes and grouped by anatomical system defects: craniofacial (anencephaly, encephalocele, hydrocephalus, spina bifida, cleft lip with/without cleft palate, anotia/microtia), cardiovascular (congenital heart defects), digestive (esophageal atresia, anal atresia), genitourinary (hypospadias, undetermined sex, bladder exstrophy), musculoskeletal (talipes equinovarus, polydactyly, syndactyly, limb reduction), abdominal (diaphragmatic hernia, omphalocele, gastroschisis), chromosomal (Down syndrome), and "other" (excluding the CA mentioned above).

The study consisted of maternal-child clinical and socioeconomic covariates of interest: newborn sex, maternal age (grouped in < 20, 20–24, 25–29, 30–34, and ≥ 35 years), residence (considering an administrative criterion, urban was defined as those participants living within Durango city, linked to postal codes 34000–34299 for more than one year before pregnancy, otherwise defined as rural), and socioeconomic status (ability to provide well-being for household members through the Mexican Association of Market Intelligence and Opinion Agencies, AMAI) (*21*).

2.3. Socioeconomic status measurement

A six-item questionnaire was used to produce an estimate of socioeconomic level based on participant's clinical records, as well as supplemented by direct interviews (particularly among CA) to avoid bias and verify background data. The items include: *a*) highest educational level of the head of household (none–master's/doctorate, 0–101 points); *b*) number of bathrooms including shower, sink, and toilet (none–two, 0–47 points); *c*) number of cars / trucks / vans (none–two, 0–37 points); *d*) internet connection (no–yes, 0–31 points); *e*) number of individuals who are employed ≥ 14 years old (none–four, 0–61 points); and *f*) number of bedrooms (none–four, 0–23 points) (*21*).

Then, a series of points were assigned, which were added and compared with the cut-off points to establish the respective household to its corresponding socioeconomic level: A/B (202–300 points), C+ (168–201 points), C (141–167 points), C- (116–140 points), D+ (95–115 points), D (48–94 points), and E (0–47 points); with higher scores indicating more favorable socioeconomic status. Regarding the cut-off points defined by AMAI, to prevent biasing from extreme data incorporated into the algorithmic and statistical model, maximum scores were distributed proportionally to 95th percentile of the distribution of each variable as stated by 2020 Mexican National Survey of Household Income and Expenses database (*21,22*).

2.4. Statistical analysis

Data were expressed as number (*n*) and percentage (%) with an estimation of the 95% confidence interval (CI). Hospital-based prevalence was calculated as the total number of CA (numerator) divided by the total number of live births (denominator), including an adjusted calculation for all CA subtypes and grouped anatomical system defects. Associations between CA and newborn sex, maternal age, residence, and socioeconomic status were analyzed using Pearson's chi-squared test and Fisher's exact test as appropriate. Subgroup analysis was performed using regression models adjusted to covariates

of interest and grouped anatomical system defects (due to the small number of events). Probability of CA and specific categories were estimated based on logistic regression analysis to identify independently associated variables, and were expressed through odds ratios (OR) along with 95% CI. All tests were two-sided with statistically significant p values of < 0.05. Data analysis was performed employing SPSS version 21 software (IBM, Armonk, New York).

3. Results and Discussion

3.1. Hospital-based prevalence of congenital anomalies and anatomical system defects

A total of 6,784 newborns without major CA and 306 newborns with at least one major CA were considered. Overall hospital-based prevalence of CA was 4.5% (95% CI: 4.0%–5.0%) and spina bifida was the most frequent (13.0%, n = 40, 95% CI: 9.3%–16.8%). Furthermore, craniofacial defects were the most prevalent with 36.9% (n = 113, 95% CI: 31.5%–42.3%), followed by musculoskeletal and "other" 15.0% (n = 46, 95% CI: 11.0%–19.0% respectively), cardiovascular 12.7% (n = 39, 95% CI: 9.0%–16.5%), digestive 7.1% (n = 22, 95% CI: 4.3%–10.1%), abdominal 5.5% (n = 17, 95% CI: 3.0%–8.1%), genitourinary 3.9% (n = 12, 95% CI: 1.7%–6.1%), and chromosomal 3.5% (n = 11, 95% CI: 1.5%–5.7%). Distribution of CA subtypes is presented in Supplementary Table S1 (*https://www.irdrjournal.com/action/getSupplementalData.php?ID=296*).

The hospital-based prevalence of CA was found to be higher (4.5%) in relation to the reported global prevalence (3%). However, estimations on CA may vary (1–5%) despite the differences in sample sizes, methodologies, or geographical settings (*1*). In this study, the single-center design may account for this outcome, whereas other plausible influences may include polygenic defects, gene-environment interactions, racial composition, or sources of CA ascertainment across studies (*2-4*).

3.2. Associations of congenital anomalies with maternal-child clinical and socioeconomic factors

Analysis of CA and maternal-child clinical and socioeconomic variables is depicted in Table 1. Variables associated with CA included male sex (OR = 1.26, 95% CI: 1.01–1.58, p = 0.048), maternal age < 20 and ≥ 35 years (OR = 1.83, 95% CI: 1.22–2.76, p = 0.017 and OR = 1.43, 95% CI: 1.02–2.01, p = 0.038, respectively), urban residence (OR = 1.82, 95% CI: 1.45–2.29, p < 0.001), and socioeconomic levels D and E (OR = 1.81, 95% CI: 1.04–3.15, p = 0.031 and OR = 3.69, 95% CI: 1.93–7.02, p < 0.001, respectively).

Notwithstanding the identified associations, it must be noted that these cross-sectional findings limit causal inference. To address this, an individual approach to these associations is discussed.

3.3. Subgroup analysis according to newborn sex

Supplementary Table S2 (*https://www.irdrjournal.com/action/getSupplementalData.php?ID=296*) shows the subgroup analysis between anatomical system defects and newborn sex. Males were more frequently associated with cardiovascular and genitourinary defects compared to females (OR = 2.23, 95% CI: 1.13–4.42, p = 0.023 and OR = 8.94, 95% CI: 1.13–70.6, p = 0.021, respectively). There were no statistically significant differences among the rest of categories.

Findings in this study diverge from a study of male and female twins with similar risks for cardiovascular defects (*10*), but are in agreement with a population-based study suggesting a greater risk for CA among males (*5*). In addition to disparities in the methodological design, clearly, sample sizes in the former are not as extensive as in the latter. Also, these differences may be influenced by hormonal and other physiologic differences in male/female embryos after gonadal differentiation, in which the effects of testosterone may be critical for strength of fetal connective tissue (*5,10*). Additionally, the overwhelming prevalence of genitourinary defects is probably etiologically related to development of the male reproductive system (*5,10*). These patterns of CA may be female biased and suggest that sex influence may also take place during early blastogenesis (*23*). Combined, these disparities may provide a hint about the relationship between sex and CA.

Table 1. Analysis of congenital anomalies and maternal-child clinical and socioeconomic variables

Variable	Congenital Anomalies, *n* (%)		OR (95% CI)
	Yes	No	
Newborn sex			
Male	170 (55.5)	3402 (50.1)	1.26 (1.01–1.58)*
Female	134 (43.7)	3382 (49.8)	Reference
Residence			
Urban	152 (49.6)	2381 (35.0)	1.82 (1.45–2.29)**
Rural	154 (50.3)	4403 (64.9)	Reference
Maternal age (years)			
< 20	39 (12.7)	568 (8.3)	1.83 (1.22–2.76)*
20–24	64 (20.9)	1714 (25.2)	0.87 (0.62–1.22)
25–29	80 (26.1)	1875 (27.6)	Reference
30–34	61 (19.9)	1615 (23.8)	0.88 (0.63–1.24)
≥ 35	62 (20.2)	1012 (14.9)	1.43 (1.02–2.01)*
Socioeconomic status			
A / B	15 (4.9)	542 (7.9)	Reference
C+	24 (7.8)	746 (11.0)	1.16 (0.60–2.23)
C	42 (13.7)	1017 (14.9)	1.49 (0.82–2.71)
C-	46 (15.0)	1085 (16.0)	1.53 (0.84–2.76)
D+	52 (16.9)	1153 (17.0)	1.62 (0.90–2.92)
D	99 (32.3)	1967 (28.9)	1.81 (1.04–3.15)*
E	28 (9.1)	74 (4.0)	3.69 (1.93–7.02)**

Notes: * p value < 0.05; ** p value < 0.01. *Abbreviations*: OR, odds ratio; CI, confidence interval.

3.4. Subgroup analysis stratified by residence

Subgroup analysis among the anatomical system defects and residence is shown in Supplementary Table S3 (*https://www.irdrjournal.com/action/getSupplementalData.php?ID=296*). In contrast to the rural area, urban residence was significantly associated with craniofacial defects (OR = 2.89, 95% CI: 1.98–4.24, $p < 0.001$), cardiovascular defects (OR = 3.32, 95% CI: 1.72–6.41, $p = 0.001$), genitourinary defects (OR = 3.69, 95% CI: 1.11–12.20, $p = 0.031$), and abdominal defects (OR = 3.39, 95% CI: 1.25–9.17, $p = 0.018$). There were no statistically significant associations in other anatomical system defects.

Benavides *et al*. identified several CA that were less prevalent in rural areas (*7*). These urban-rural differences may be related to several factors or surveillance of CA. For instance, multiple pesticides exposure in the urban environment is employed for industrial and indoor pest control. While parental exposure to pesticides and agricultural compounds (nitrate, atrazine, and desethylatrazine detected in drinking water) may be associated with CA, notably hypospadias (*24,25*). Furthermore, due to the increased concentrations of several pollutants, such as particulate matter (≤ 10 and ≤ 5 μm), carbon monoxide, nitrogen dioxide, and ozone, urban air pollution has been associated with CA, namely cardiovascular defects (*26*). It is unknown whether women in this study were systematically different due to the inherently cross-sectional design. Further research will be required to assess these factors.

3.5. Subgroup analysis regarding maternal age

Compared to mothers between 25–29 years, craniofacial and abdominal defects were significantly associated among mothers < 20 years (OR = 2.09, 95% CI: 1.16–3.74, $p = 0.016$ and OR = 3.96, 95% CI: 1.20–13.02, $p = 0.024$, respectively). Meanwhile, advanced maternal age (≥ 35 years) seems highly associated with digestive and chromosomal abnormalities (OR = 3.33, 95% CI: 1.11–9.97, $p = 0.044$ and OR = 11.10, 95% CI: 1.33–92.4, $p < 0.001$, respectively) (Supplementary Table S4, *https://www.irdrjournal.com/action/getSupplementalData.php?ID=296*). No statistically significant associations were found in other anatomical system defects.

As previously reviewed (*6*), results in this study support the striking evidence between maternal age and CA, namely, chromosomal abnormalities. Of note, Down syndrome within the current analysis as part of those clinically recognizable disorders was included, even though it is not a birth defect but rather a genetic syndrome. In contrast, a decreased effect of advanced maternal age among CA has been reported (*9*). Gametogenesis in females begins before birth and may take a long time to be completed (*e.g.* up to 45 years). Such biological scenarios, represent a sizable window of susceptibility to telomere shortening, increased oxygen free radical levels, or errors in sister chromatid segregation from early exposure to tobacco, alcohol, and illicit drugs, or nutrient deficiencies affecting normal chromosomal differentiation of oocytes (*6,9*). The methodological design in this study prevents relating such influences to the occurrence of CA.

3.6. Subgroup analysis across socioeconomic status

Compared to level A/B (highest), levels D and E were more frequently associated with craniofacial defects (OR = 2.59, 95% CI: 1.02–6.54, $p = 0.039$ and OR = 3.95, 95% CI: 1.33–11.65, $p = 0.011$, respectively). Moreover, cardiovascular defects were highly associated with socioeconomic level E (OR = 6.92, 95% CI: 1.42–33.5, $p = 0.009$) (Supplementary Table S5, *https://www.irdrjournal.com/action/getSupplementalData.php?ID=296*). Other categories did not show a systematic variation in the association with anatomical system defects through socioeconomic levels.

Adverse socioeconomic status among a wide range of CA has been shown to be associated with cardiac and digestive anomalies (*8*), as well as craniofacial and cardiovascular defects among the Hispanic population (*14-19*). Such associations may be related to social and prenatal care inequalities as well as maternal psychosocial factors (*2-4,11*). Despite socioeconomic status having multiple dimensions; no single indicator can encompass all perspectives and represents a diverse set of factors in different populations (*27*). Socioeconomic findings reflect components as measured by education, basic infrastructure, and human capital among the current Mexican households that might influence the current results. It should be noted that near to 60% of CA were distributed between levels D+, D, and E, which are deemed as the lowest socioeconomic status according to AMAI (*21*). Although these cross-sectional findings preclude causality, women in this study may experience heterogeneous socioeconomic and health circumstances, leading to low educational attainment, unemployment, household crowding, poverty, or a limited-resource setting (*28,29*). Such sources might provide clues about social influences in CA.

3.7. Limitations and strengths

First, there is a possibility of underdiagnosing of CA among cardiovascular and renal anomalies and stillbirths were not examined for this study. Such instances may be diagnosed after the neonatal period or could represent cases of stillbirth due to the type of anomaly and hence, providing a potential source of bias. Likewise, some subgroups anomalies (*e.g.*, genitourinary and chromosomal anomalies) may also be subject to early fetal demise and the number of events was small; therefore, the CI were wide potentially limiting

interpretation of the magnitude of the effect size. Caution is recommended concerning overinterpretation of these findings.

Second, analysis for specific birth defects was not carried out. Yet, subgroup analysis by anatomical system defects were performed, obtaining noteworthy results which might aid for clinical CA disparities prevention. Third, there may be unmeasured individual-level environmental components, as residence and the socioeconomic status environment fluctuate over time; therefore, it cannot be assured to its exact boundaries. Caution should be considered when interpreting these results. Finally, the cross-sectional design restricts causal inference, whereas current findings from a single hospital-based setting may not be generalizable to other ethnicities. Thus, the relationship mechanisms between these associations are speculative. However, given that a wide range of CA was explored and most of these phenotypes are rare with an unknown etiology, the sample size was sufficient for examining maternal-child clinical and socioeconomic disparities.

Strengths include the well-characterized hospital-based ascertainment of cases and its standardized diagnostic of a comprehensive range of CA. Further strength is the employment of socioeconomic levels by AMAI, which is based on a Mexican conceptual framework considering the Mexican National Survey of Household Income and Expenses database (*21,22*). This validated socioeconomic index was available for all studied mother-child pairs, consequently, it was possible to maximize sample size and improve precision of results.

4. Conclusions

Prevalence of CA in this hospital-based setting indicate that sex, maternal age, residence, and socioeconomic differences are common. Increased associations to male sex, young and advanced maternal age, urban residence, and adverse socioeconomic status may be used as proxies for epidemiological characteristics associated with several CA. The latter suggests complex gene-environment interactions in CA; though the cross-sectional design limits generalizability and causality on this topic. By examining the hospital-based prevalence of these CA, this study research may support the development of preventive strategies including maternal age-, residence-, and socioeconomic-specific features. These findings provide region-detailed epidemiological evidence that might be relevant to maternal-child health and reduce the occurrence of CA in the future.

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