Congenital Anomalies: Prevalence and Risk Factors

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Abstract   Objective: The aim of this study is to assess the incidence, types and correlates of congenital anomalies (CA) among stillborn and liveborn infants in two Lebanese hospitals in Mount-Lebanon. Methods: In this cross-sectional study, all the newborns who were born during 9 months period from January to December 2009 (n=1000) at two hospitals setting in Mount-Lebanon hospital, Lebanon were studied. The newborns were assessed for CA. Neonatal data were extracted from medical records of the nursery. The classification of malformations was based upon the anatomical system affected according to the WHO classification of CA. Results: Of the all 1000 single births, 24 (2.4%) were diagnosed as being congenitally malformed. Cardiovascular system defects and limbs anomalies (4/1000) were mostly detected, followed by genitourinary system (2/1000), nervous system (2/1000), respiratory system (2/1000) malformations and chromosomal anomalies (1/1000). A marked association of parental consanguinity and alcohol consumption of the mother during the pregnancy with increased CA rates was found (p= 0.015 and p=0.027 respectively). Conclusions: The frequency of malformations in the study was approximately similar to previous investigations. The increased incidence of CA in cases of parental consanguinity prompts the necessity of establishing educational programs to avoid these complications in the offspring.

Keywords   Newborn, Defects, Epidemiology, Consanguinity, Lebanon

1. Introduction

Congenital anomalies (CA) can be defined as structural or functional abnormalities including metabolic disorders, present at birth. These defects of prenatal origin result from defective embryogenesis or intrinsic abnormalities in the development process. Birth defects can be isolated abnormalities or part of a syndrome and continue to be an important cause of neonatal and infant morbidity and mortality [1, 2].

Based on the World Health Organization (WHO) report, about 3 million fetuses and infants are born each year with major CA. They are found in approximately 3% of newborns [3]. Worldwide surveys have shown that birth prevalence of congenital anomalies varies greatly from country to country. It is reported to be as low as 1.07% in Japan and as high as 4.3% in Taiwan [4]. In the US, a 2-3% birth prevalence of congenital anomalies has been reported. The birth prevalence of congenital anomalies in England is 2% and in South Africa it is 1.49% [5]. In Lebanon, the incidence of major congenital anomalies has been reported as 1.64 % in Southern Beirut [6]. The variation in rates may be explained by social, racial, ecological, and economical influences [4, 5]. The most common serious congenital disorders are congenital heart defects [7], neural tube defects [8] and Down syndrome [9].

CA can be a cause of infant mortality; among infants with malformation who do not survive, more than 70% die in the first month of life. Approximately 40% to 60% of CA are of unknown origin. The etiology of Congenital Malformation is genetic (30-40%) and environmental (5 to 10%). Among the genetic etiology, chromosomal abnormality constitutes 6%, single gene disorders 25% and multifactorial 20- 30%; however, for nearly 50% of CA, the cause is yet to be known [10]. Consanguineous marriages have been described as an important factor contributing to increased CM. Studies have shown a significantly higher incidence of malformations in offspring of consanguineous parents [11].

The main objective of this study is to establish the prevalence and pattern of CA in neonates in two hospitals in Mount Lebanon between January 2009 and December 2009, and to evaluate their correlates, in order to identify the appropriate strategies for prevention.

Accurate quantification of congenital anomalies within a given population is essential for estimating their burden and documenting the need for prevention, for public health policy development, for planning and implementation of services needed by children with malformations and for evaluating the effects of preventive measures and treatment services. Differences in birth defect rates in different countries and studies could be attributed to true differences among different populations or to different definitions of
birth defects, different methods, and different time periods for ascertainment.

2. Methods

2.1. Type of the Study

This is a retrospective hospital based records, cross-sectional study with consecutive sampling of newborns babies, who had been delivered in two Lebanese Hospital, based in Mount-Lebanon, Lebanon. These hospitals serve mainly urban areas in the region and were therefore chosen as an example of an average public health maternity hospital. The survey included 1000 neonates delivered between January 2009 and December 2009. All the charts identified from the Medical Birth Registry of the deliveries taking place at the hospital were reviewed for the presence of CA, based on medical records of antenatal care, delivery care, and pediatric examination of the newborn [12]. All singletons newborns delivered in this hospital during the study period were examined at birth and screened for major CA.

Variables recorded included demographic data: date of birth, sex of the newborn and age of the mother as well as weight, length, head circumference and apgar scores of the newborn [13].

Malformations were classified into systems according to World Health Organization (WHO) recommendations [11]. The abnormalities were divided into several groups relative to the following systems: Genitourinary, Musculoskeletal, Nervous, Gastrointestinal, Cardiovascular and Pulmonary systems and to limbs abnormalities and miscellaneous disorders.

2.2. Statistical Analysis

Data were entered and analyzed using SPSS, version 18.0. Descriptive results were presented using mean and standard deviation for continuous variables and percentages for qualitative variables. Bivariate analyses were also conducted: Chi-square test was used to compare between two or more percentages when fulfillment conditions were satisfied. When an expected count was lower than 5 in a cell, Fisher Exact test was used. In addition, Student test was used to compare between two means, after ensuring that variances were homogeneous in both groups of comparison.

Multivariate analyses were carried out: when the dependent variable was dichotomous, a logistic regression was performed using a stepwise descending likelihood ratio method; here we used the Hosmer & Lemeshow test to ensure sample adequacy. When the dependent variable was quantitative, we used a multiple regression using the stepwise method, after ensuring residual normality, homoscedasticity and absence of colinearity.

Malformation, apgar score, baby’s weight and cranial perimeter were considered as dependent variables whereas baby’s sex, parental consanguinity, mother’s professional status, sibling’s malformation, mother’s smoking during pregnancy, mother’s alcohol consumption during pregnancy, baby conception by in vitro fertilization, prematurity, birth by caesarean section, mother’s iron intake during pregnancy, mother’s calcium intake during pregnancy, mother’s vitamins intake during pregnancy, mother’s drug intake during pregnancy, mother’s gestity, number of abortions, number of children and mother’s age were taken as independent variables. Stillbirth was also taken as a dependent variable, with similar independent variables as above, in addition to the major independent variable of congenital malformation.

3. Results

3.1. Sample Description

One thousand births were recorded: 862 (86.2 %) in the one hospital, and 138 (13.8 %) in the other hospital. 512 (51.2%) were males and 488 (48.8%) were females. Out of 1000 births, 24 (2.4%) had a malformation, while 44 (4.4%) were stillborn or died perinatally. No information was available about 2 birth (0.2%).

The mean maternal age was observed to be 25.97±9.7. 632 (63.2%) and 368 (36.8%) newborns were delivered by natural vaginal delivery (NVD) and cesarean section (CS) respectively.

The prevalence of CA among 1000 hospital live births was 2.4% (24/1000 total births). The frequency distribution of the 24 cases of newborns with birth defects according to the diagnosis of the affected system or abnormality is shown in Table 1. The commonest detected anomalies were those of the congenital cardiovascular disease (16.6%) and limb anomalies (16.6%); polydactyly (12.5%) and abnormal palmar creases (4.16%). Musculoskeletal system, genitourinary system, central nervous system and respiratory system involved 8.4% of the cases for each system. Chromosomal anomalies represented by Down’s syndrome, were found in 1 of the 24 CA cases (4.16%).

3.2. Comparison between Births with and without Congenital Malformation

Parents’ consanguinity (p=0.015), mother’s alcohol consumption during pregnancy (p=0.027), stillbirth or perinatal death (p=0.001), and mother’s drugs intake during pregnancy (p<0.001) were all positively associated with congenital malformation; meanwhile, mother’s calcium intake during pregnancy (p=0.013) was inversely associated with congenital malformation (Table 2).
### Table 1. Systemic distribution and percentage of congenital malformations (CA) among 1000 birth

| Malformation/System          | Number of births with the corresponding malformation (24 cases) | Percentage of distribution of the corresponding malformation (24 cases) |
|-----------------------------|---------------------------------------------------------------|---------------------------------------------------------------------|
| Cardiovascular system       | 4                                                             | 16.66                                                               |
| Nervous system              | 2                                                             | 8.4                                                                 |
| Respiratory system          | 2                                                             | 8.4                                                                 |
| Genitourinary system        | 2                                                             | 8.4                                                                 |
| Musculoskeletal system      | 2                                                             | 8.4                                                                 |
| Anomalies of limbs          | 4                                                             | 16.66                                                               |
| Eye, ear, face, Neck        | 1                                                             | 4.1                                                                  |
| Behcet syndrome             | 1                                                             | 4.1                                                                  |
| Cephalohematoma             | 1                                                             | 4.1                                                                  |
| Chromosomal Abnormalities   | 1                                                             | 4.1                                                                  |
| Miscellaneous               | 4                                                             | 16.66                                                               |
| Total                       | 24                                                            | (100%)                                                               |

### Table 2a. Characteristics related to births with or without congenital malformations

| Characteristics                          | No congenital malformation N=974 (97.6%) | Congenital malformation N=24 (2.4%) | p-value | Total N=998 |
|------------------------------------------|------------------------------------------|-------------------------------------|---------|-------------|
| Hospital                                 |                                          |                                     |         |             |
| 1                                        |                                          |                                     |         |             |
| 2                                        |                                          |                                     |         |             |
| Females                                  | 476(97.9%)                               | 10(2.1%)                            | 0.485   | 486         |
| Males                                    | 498(97.3%)                               | 14(2.7%)                            |         | 512         |
| Consanguinity of Parents                 |                                          |                                      |         |             |
| No                                       | 790(98.3%)                               | 14(1.7%)                            | 0.015*  | 804         |
| First degree                             | 123(94.6%)                               | 7(5.4%)                             |         | 130         |
| Second degree or more                    | 61(95.3%)                                | 3(4.7%)                             |         | 64          |
| Mother works                             |                                          |                                      |         |             |
| No                                       | 936(97.6%)                               | 23(2.4%)                            | 0.620*  | 959         |
| Yes                                      | 38(97.4%)                                | 1(2.6%)                             |         | 39          |
| Siblings malformation                    |                                          |                                      |         |             |
| No                                       | 941(97.5%)                               | 24(2.5%)                            | 1.000   | 965         |
| Yes                                      | 33(100%)                                 | 0                                   |         | 33          |
| Smoking mother during pregnancy          |                                          |                                      |         |             |
| No                                       | 790(97.8%)                               | 18(2.2%)                            | 0.433   | 808         |
| Yes                                      | 184(96.8%)                               | 6(3.2%)                             |         | 190         |
| Mother consumed alcohol during Pregnancy |                                          |                                      |         |             |
| No                                       | 964(97.8%)                               | 22(2.2%)                            | 0.027   | 986         |
| Yes                                      | 9(81.8%)                                 | 2(18.2%)                            |         | 11          |
| Baby conception by In vitro fertilization|                                          |                                      |         |             |
| No                                       | 969(97.6%)                               | 24(2.4%)                            | 1.000   | 993         |
| Yes                                      | 5(100%)                                  | 0                                   |         | 5           |
| Premature birth                          |                                          |                                      |         |             |
| No                                       | 693(98.0%)                               | 14(2.0%)                            | 0.170   | 707         |
| Yes                                      | 280(96.6%)                               | 10(3.4%)                            |         | 290         |
| Birth by Caesarean section               |                                          |                                      |         |             |
| No                                       | 618(97.9%)                               | 13(2.1%)                            | 0.351   | 631         |
| Yes                                      | 356(97.0%)                               | 11(3.0%)                            |         | 367         |
| Stillbirth or perinatal death            |                                          |                                      | <0.001  | 955         |
| No                                       | 937(98.1%)                               | 18(1.9%)                            |         | 43          |
| Yes                                      | 37(86.0%)                                | 6(14.0%)                            |         |             |
| Mother took iron during pregnancy        |                                          |                                      |         |             |
| No                                       | 146(95.4%)                               | 7(4.6%)                             | 0.079   | 153         |
| Yes                                      | 827(98.0%)                               | 17(2.0%)                            |         | 844         |
| Mother took calcium during pregnancy     |                                          |                                      |         |             |
| No                                       | 202(95.3%)                               | 10(4.7%)                            | 0.013   | 212         |
| Yes                                      | 727(98.2%)                               | 14(1.8%)                            |         | 786         |
| Mother took vitamins during pregnancy    |                                          |                                      |         |             |
| No                                       | 831(97.3%)                               | 23(2.7%)                            | 0.236   | 854         |
| Yes                                      | 143(99.3%)                               | 10(0.7%)                            |         | 144         |
| Mother took other drugs during Pregnancy |                                          |                                      | <0.001  | 853         |
| No                                       | 839(98.4%)                               | 14(1.6%)                            |         | 853         |
| Yes                                      | 135(93.1%)                               | 10(6.9%)                            |         | 145         |
Table 2b. Characteristics of births with and without congenital malformation (continued)

| Characteristics                        | No congenital malformation | Congenital malformation | p-value |
|----------------------------------------|---------------------------|-------------------------|---------|
|                                        | N=974                     | N=24                    |         |
|                                        | Mean (SD)                 | Mean (SD)               |         |
| Mother’s age                           | 28.54(6.02)               | 28.74(6.30)             | 0.874   |
| Mother’s gestity                       | 2.65(1.74)                | 2.96(2.03)              | 0.387   |
| Mother’s number of abortions           | 0.69(1.10)                | 0.92(1.14)              | 0.323   |
| Mother’s number of live children       | 1.64(1.36)                | 1.58(1.53)              | 0.847   |
| Weight of the baby (in kg)             | 3154.98(477.11)           | 2908.95(584.02)         | 0.027   |
| Height of the baby (in cm)             | 49.62(2.35)               | 48.56(3.03)             | 0.058   |
| Cranial perimeter of the baby (in cm)  | 33.97(1.77)               | 33.44(1.72)             | 0.209   |
| Apgar score at 5 min                   | 8.80(1.82)                | 5.71(3.63)              | <0.001  |

Table 3. Multivariate analyses of congenital malformations and other birth characteristics

| Dependent variables | Independent variables | ORa/Beta | [95% CI] | p-value | R² | H-L* |
|---------------------|-----------------------|----------|----------|---------|----|-----|
| Congenital malformation | Parents consanguinity | 1.72     | 0.94;3.15 | 0.078   | 0.10 | 0.629 |
|                     | Mother’s consumption of alcohol | 10.42 | 1.91;56.73 | 0.007   |     |     |
|                     | Mother’s consumption of drugs | 5.23     | 2.20;12.42 | <0.001  |     |     |
| Perinatal birth/stillbirth | Congenital malformations | 7.63     | 2.67;21.79 | <0.001  | 0.16 | 0.551 |
|                     | Caesarean section delivery | 1.86     | 0.98;3.55  | 0.058   |     |     |
|                     | Lower gestity           | 1.72     | 1.23;2.38  | 0.001   |     |     |
|                     | Mother’s number of abortions | 1.73     | 1.13;2.66  | 0.013   |     |     |
| Apgar score         | Mother’s number of live children | 0.16     | 0.07;0.25  | <0.001  | 0.04 | NA   |
|                     | Mother’s smoking during pregnancy | -0.45    | -0.76;0.15 | 0.004   |     |     |
|                     | Mother’s vitamins intake | 0.54     | 0.20;0.89  | 0.002   |     |     |
|                     | Mother’s iron intake    | 0.40     | 0.06;0.73  | 0.020   |     |     |
|                     | In vitro Fertilization conception | -1.79   | -3.49;0.10 | 0.038   |     |     |
|                     | Parents’ consanguinity  | -0.22    | -0.44;0.01 | 0.048   |     |     |
| Baby’s weight       | Mother’s smoking        | -236.74  | -313.91;159.57 | <0.001 | 0.04 | NA   |
|                     | Caesarean section delivery | -74.03   | -136.72;11.35 | <0.001 |     |     |
| Baby’s cranial perimeter | Siblings congenital malformation | 1.52 | 0.84;2.19 | <0.001 | 0.05 | NA   |
|                     | Mother’s number of abortions | 0.19     | 0.07;0.30  | 0.001   |     |     |
|                     | Mother’s smoking        | -0.34    | -0.63;0.06 | 0.019   |     |     |
|                     | Prematurity              | -0.26    | -0.51;0.01 | 0.042   |     |     |

*H-L: Hosmer & Lemeshow test for sample adequacy

However, hospital, sex, mother’s working status, siblings, congenital malformation, mother’s smoking during pregnancy, baby’s conception by in vitro fertilization, premature birth, birth by caesarean section, and mother’s iron and vitamins intakes during pregnancy were not significantly associated with congenital malformation (p>0.05) (Table 2).

Moreover, congenital malformation was significantly associated with relatively low weight of the baby (p=0.027) and relatively low Apgar scores at 5 minutes (p<0.001). However, mean mother’s age, gestity, number of abortions and of live children, and baby’s cranial perimeter did not significantly when comparing between babies with or without congenital malformation. Additionally, concerning baby’s height, there was a trend towards lower height in babies with congenital malformation (p=0.058) (Table 2).

3.3. Multivariate Analyses

Parents consanguinity (ORa=1.72), mother’s consumption of alcohol and drugs (ORa=10.42, ORa=5.23 respectively) were associated with higher risk of congenital malformation. Factors correlated with perinatal death/stillbirth included CA (ORa=7.63), delivery by caesarean section (ORa=1.86), mother’s lower gestity (ORa=1.72) and increased number of abortions (ORa=1.73) (Table 3).

Apgar score correlates positively to mother’s number of live children, vitamins and iron intakes during pregnancy;
whereas, it was significantly decreased by mother’s smoking during pregnancy, in vitro fertilization and parents’ consanguinity. Baby’s weight was negatively affected by mother’s smoking during pregnancy and inversely correlated to the caesarean section delivery. Baby’s cranial perimeter was increased by siblings’ CA, mother’s number of abortions; and was decreased by mother’s smoking during pregnancy and prematurity. However, for all models, the dependent variables variance percentages explained by the model were relatively low.

4. Discussion

Our population-based study involved 1000 newborns in 2 hospitals in Mount-Lebanon between January and December 2009. Our data was based on the hospital's medical records. Out of 1000 infants, 24 were born with CA, thereby the incidence rate of CA is 2.4%. Most of the malformed stillbirths in the present study were cases with cardiovascular congenital anomalies (16.6%) and limb anomalies (16.6 %) including polydactyly (12.2%) and abnormal palmar crease (4.16%). Previous reports on the incidence of congenital anomalies in different populations show similar rates reported by Libyan Arab Jamahiriya [14] and Oman [15], Spain [16], Iran [17] and India [18]. The frequency of CA in our study was lower than that reported by Saudi Arabia [19] and Egypt [4]. However, it was higher than the frequencies reported in Kuwait [16], UAE [15] and the region of West Beirut [6]. All incidences reside within the same range and without differences.

Consanguinity is important factor which was found to increase the risk of CA [20-22]. In Lebanon, as in Middle Eastern communities, consanguinity is high [23]. This study reports a significant positive association between the consanguinity and CA in the Lebanese population.

Many studies have demonstrated male predominance amongst congenital malformed babies. In our study, the gender of the fetus had no effect on the incidence of CA, which concurs with the findings of Lei [24] and both genders are equally distributed [5, 24].

Maternal age is an important parameter in the birth of a congenitally malformed fetus [25]. In Turkey, studies show that 5.2% of the mothers are older mothers (35 years of age or older) [26] and 8.7% of anomalous births were from older mothers, although this was not statistically significant [25]. However in our study this correlation was not evident. It may be due to the relatively small number of cases included in the study with the percentage of women being above 35 years 14.1 % (141/999) giving birth to 8.33 % (2/24) of malformed fetuses vs 84.4 % (844/999) of the women being between 18-35 y and giving birth to 87.5 % (21/24) of malformed fetuses.

Because of the high frequency of cardiovascular defects as revealed by our investigations, we recommend their proper prenatal diagnosis both by abdominal sonography and echocardiography. We thus recommend that all neonates should be thoroughly examined and investigated for CA. In addition, a Lebanese registry of CA is needed; appropriate health education about consanguinity and genetic counseling for consanguineous couples should also be established before marriage.

In addition to this, there is a need for more extensive, nationwide screening studies to determine the birth prevalence, types and distribution of congenital anomalies in the Lebanese population and the establishment of an ongoing surveillance system for congenital anomalies.

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