The impact of environmental factors on the occurrence of congenital heart disease in the form of hypoplastic left heart syndrome

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Abstract

Introduction: Congenital heart defects are the most common abnormalities in neonatal age. Congenital heart defects occur with a frequency of 3-12/1000 births. A special group is constituted by children with hypoplastic left heart syndrome because their treatment is extremely complex, requiring threestage surgery and the involvement of various specialists.

Material and methods: We analysed 100 infants with congenital heart defects in the form of hypoplastic left heart syndrome (HLHS). They were compared with a control group of 100 newborns without structural heart defects. The children's parents were asked to fill out a questionnaire consisting of 10 simple questions. It had been constructed in consultation with a psychologist in order not to offend the feelings of the parents affected by the illness of their offspring.

Results: Congenital heart defects were present in the family medical histories of 16 HLHS children and 11 healthy children (p = 0.4). Genetic disorders were present in the family medical histories of 13 HLHS children and 15 healthy children (p = 0.73). In the HLHS group, the mothers smoked cigarettes or were exposed to tobacco smoke in 32% of cases; in the control group, this proportion amounted to 23% (p = 0.76).

Conclusions: The study found no relationship between the occurrence of hypoplastic left heart syndrome in children and the parents’ age, the presence of genetic disorders, or heart defects in the family medical histories.

Key words: congenital heart disease, HLHS, environmental factors.

Introduction

Heart defects are among the most common congenital defects in neonates. The incidence of congenital heart defects is estimated at 3-12 per 1000 births. This risk rises two-fold for premature infants. The congenital heart defects that are most frequently treated with surgery include ventricular septal defect, atrial septal defect, and patent ductus arteriosus [1].

The causes of heart defects remain unknown in 90% of cases. The factors that may influence their occurrence

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are widely considered to include genetic disorders, viral infections during pregnancy, the use of some types of medication and alcohol, and uncontrolled diabetes in the mother [2-5].

Epidemiological studies confirm the influence of the mother’s exposure to polluted air on the occurrence of a congenital heart defect in the child [6-16]. Notwithstanding, the causes for the occurrence of many developmental defects, including hypoplastic left heart syndrome, remain unknown.

**Material and methods**

The study analysed 100 cases of live-born neonates with hypoplastic left heart syndrome and compared them with a control group of 100 neonates without structural heart defects by conducting an anonymous voluntary questionnaire among the children’s parents. The questionnaire included 10 simple questions. A psychologist was consulted in order to avoid hurting the feelings of parents affected by the illness of their offspring. The questionnaire was conducted among the parents of the study group children undergoing surgery at the Clinic of Paediatric Cardiac Surgery (Collegium Medicum of the Jagiellonian University) between 2008 and 2014 and among the parents of randomly selected children free of heart defects born in obstetric wards in southern Poland.

Questionnaire:
1. Is this your first child? Yes/No
2. Please state the age of the mother.
3. Please state the age of the father.
4. Does your family’s medical history include heart defects? Yes/No
5. Does your family’s medical history include genetic disorders? Yes/No
6. Did the mother smoke cigarettes during the pregnancy/ had she been exposed to tobacco smoke? Yes/No
7. Did the mother come in contact with other harmful substances (alcohol, chemicals, inebriants)? Yes/No
8. Did the mother take any medication during the pregnancy? Yes/No
9. Is it possible that the father was under the influence of any chemical substances (medication, tobacco smoke, alcohol, chemicals, inebriants) during the period around conception? Yes/No
10. What is your standard of living? Good/Moderate/Poor

The answers to these questions were not problematic to the respondents, and they participated in the questionnaire without reservations.

Statistical analysis of the results was conducted with the use of Student’s t test and the Mann-Whitney U test (software used: Statistica 10.0). A value of \( p < 0.05 \) was assumed to be statistically significant.

**Results**

First children of their parents constituted 44% of the HLHS group and 32% of the control group (\( p = 0.09 \)). The mean age of the mothers was 27.86 ± 5.61 years in the HLHS group and 26.43 ± 5.85 years in the control group (\( p = 0.08 \)). The mean age of the fathers was 30.74 ± 5.39 years in the HLHS group and 30.12 ± 6.32 years in the control group (\( p = 0.41 \)).

Congenital heart defects were present in the family medical histories of 16 HLHS children and 11 healthy children (\( p = 0.4 \)).

Genetic disorders were present in the family medical histories of 13 HLHS children and 15 healthy children (\( p = 0.73 \)).

In the HLHS group, the mothers smoked cigarettes or were exposed to tobacco smoke in 32% of cases; in the control group, this proportion amounted to 23% (\( p = 0.76 \)).

In the HLHS group, the mothers had contact with other harmful substances in 25% of cases; in the control group, this proportion was 23% (\( p = 0.25 \)).

In the HLHS group, the mothers received medications for chronic illnesses in 25% of cases; in the control group, this proportion was 17% (\( p = 0.42 \)).

The factors that may potentially be responsible for the occurrence of heart defects in children include, among others, environmental pollution. Studies conducted by Stingone et al. have proven that women who gave birth to children with HLHS were twice as likely to live in neighbourhoods associated with higher exposure to pollutant particles ≤ 2.5 m than women who gave birth to children without this defect [18].

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The significance of the age of the mother in the development of a congenital heart defect in the child is also underscored [19]; it is an independent risk factor for the development of congenital heart defects in neonates despite the lack of chromosomal anomalies. Among our respondents, no association was found between the age of the mothers of HLHS children and the age of the mothers of non-HLHS children, nor was there any association between the age of the fathers of HLHS and non-HLHS children.
Another causative factor that may be responsible for the occurrence of a congenital heart defect in the child is the mother’s obesity. Gilboa et al. and Mills et al. reported an association between HLHS occurrence and severe obesity in the mother: BMI 30.0-34.9 kg/m² and BMI 30.0-39.9 kg/m², respectively [5, 20].

Genetic predisposition is an exceptionally important risk factor for the occurrence of congenital heart defects. Among our respondents, no statistical significance was associated with the presence of congenital heart defects in the family histories of HLHS and non-HLHS children. We also did not find any statistically significant difference between the groups regarding the presence of genetic disorders in the family. Notwithstanding, the progress made in the field of biotechnology is giving rise to an increasing number of publications investigating the genetic aspects of congenital heart defects. Menten et al. point to the relationship between the occurrence of congenital heart defects (including HLHS) and 22q11.2 microdeletion [21]. Grossfeld et al. reported that 56% of patients with Jacobsen syndrome have congenital heart defects, which very frequently includes HLHS [22].

A study conducted in Finland by Tikkanen et al. analysed 34 mothers of children with HLHS and compared them with a control group comprising mothers of randomly selected children born during the same period [23]. The study found a statistical relationship between the occurrence of upper respiratory tract infection in the mother during the first trimester of pregnancy and the development of HLHS in the child. However, it did not confirm the role of the mother’s exposure to disinfectants, pesticides, dyes, hair sprays, paints, or inhalational anaesthetics in the development of HLHS in the child. The use of deodorants and hair sprays during the first trimester of pregnancy also had no bearing on the HLHS risk. The study found no influence of the use of alcohol, coffee, or tobacco by the mother on the risk of HLHS development in the child. In turn, Sullivan et al. reported that the mother’s tobacco use is slightly or moderately associated with the development of pulmonary valve defects and atrial septal defects in the child [24]. The results of our questionnaire showed no association between HLHS development in the studied children and the use of tobacco or other harmful substances by their mothers.

The maternal status of parents of children with congenital heart defects was observed to directly influence survival [25]. The results of our questionnaire did not indicate any association between the family’s material status and the occurrence of HLHS.

Conclusions

In the studied material, no association was found between the occurrence of hypoplastic left heart syndrome in children and the parents’ age, material status, and use of medications, tobacco, and inebriants, or the presence of genetic disorders in the family medical histories.

Disclosure

Authors report no conflict of interest.

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