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Congenital Malformation Prevalence in Cluj District between 2003-2007

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Abstract: *Introduction:* Congenital anomalies represent a significant cause of premature birth, of child morbidity and mortality. From 200000 new born per year, over 10000 presented malformations. Epidemiologic studies have shown that the incidence of malformations is increasing and varies upon geographic features, race and gender. Perinatal mortality is generated in 66.66% of cases by congenital malformations, illnesses from perinatal period and the rest of them is generated by the birth. *Material and Method*: The study was retrospective and was carried on for a period of five years (2003-2007) based on medical records and on laboratory results, (especially those for TORCH screening: toxoplasmosis, rubella, cytomegalovirus, and herpes virus). *Results*: Major structural anomalies were present at 39.51% (388 cases) of 982 patients which were registered in Genetic Pathology Center from Pediatric Clinics I, Cluj-Napoca. Diagnosed abnormalities included: congenital malformations of circulatory, respiratory, digestive, central nervous system, congenital malformations of skeletal system, Down syndrome, which is consistent with results of other studies showing that the most common are heart abnormalities (33.06%), followed in descending order of frequency by urinary, genital, CNS, skin, oral-facial cleft and digestive anomalies. *Conclusions*: Early detection of major malformation during early pregnancy can indicate for medical termination of pregnancy to reduce the high morbidity and mortality of neonates due to congenital malformations. So proper and timely counselling, regular antenatal care with folate supplementation especially during the most sensitive period of embryogenesis is essential to avoid major congenital malformation for future pregnancy.

Key words: Congenital abnormalities**;** Prevalence; Morbidity.

Introduction

The research is about prevalence description of congenital anomalies observed in Cluj district and in Institute of Public Health Cluj-Napoca territory, in a determined period of time.

Congenital anomalies represent a significant cause of premature birth, of child morbidity and mortality. Structural anomalies are considered to be major when are visible to inspection, the rest of them are considered "occult".

They correspond to a large spectrum of clinical manifestation, with prenatal conditioning, despite the age of clinical debut or the age of diagnosis. They are: chromosomal abnormalities, monogenic diseases, embryo fetal diseases or belonging to dismorphic syndromes with not well known pathogenesis.

Worldwide, major congenital anomalies appear in 1-4% cases from of all births. In our country the value is 5% cases from of all births.

The danger is increasing in old woman pregnancies and in pregnancies which are not monitored. From 200000 new born per year, over 10000 presented malformations. Epidemiologic studies have shown that the incidence of malformations is increasing and varies upon geographic features, race and gender. Perinatal mortality is generated in 66,66% of cases by congenital malformations, illnesses from perinatal period and the rest of them is generated by the birth.

Etiology of congenital anomalies is not completely understood. According with multiple factor hypotheses, malformations are determined by the combination of the environmental and genetic factors. Knowing etiology is the base of prevention programs.

Material and Method

The study was retrospective and was carried on for a period of five years (2003-2007) and was based on medical records and on laboratory results (especially those for TORCH screening: toxoplasmosis, rubella, cytomegalovirus, and herpes virus).

In this study the term congenital anomalies include all types of major structural anomalies (congenital malformations, disruptions, deformations, dysplasia), chromosomal anomalies, monogenic or polygenic hereditary illnesses and undefined anomalies.

The only criterion for inclusion in the study was the presence of a congenital malformation with or without associated malformations. Anomalies were codified according to CID-10. The analysis refers to the number of cases from a category of anomalies and not to the anomalies number.

The moment of anomalies discover was the criterion of cases grouping. Following aspects were analyzed: age of the moment of diagnosis establishment, gender, family history of illness, mother physiologic history, type of malformation.

For local data the source was represented by Ist and IInd Obstetrics and Gynecology Clinics Cluj-Napoca. For the rest of data the source was Statistic Yearbook of Romania and brochures of CNOASIIDS Bucharest.

Statistic analysis was performed with Excel (Microsoft Office 2003) and EpiInfo (3.5.1. version) and included χ^2 test and prevalence. Graphical representations were done with Excel (Microsoft Office 2003).

Results

Analysis of Distribution of Congenital Anomalies Cases in Cluj District in 2003-2007 Period of Time, in Relation with the Residence Environment, Gender and Age

In investigated five years of the study, in the Obstetrics and Gynecology Clinics in Cluj Napoca were registered 30942 births (16033 males and 14909 females). In the same period of time there were 388 new cases with anomalies diagnosis. From these, 157 (40.46%) were diagnosed at birth.

In Table 1 is presented the number of new cases of congenital anomalies.

Table 1. Congenital malformation diagnosed in period 2003-2007 in Cluj district

Year	Live Births			New cases of congenital anomalies	Congenital anomalies diagnosed at birth
	Total	Male	Female		
2003	5668	2959	2709	102	50
2004	5976	3054	2922	79	34
2005	6420	3358	3062	61	31
2006	6601	3407	3194	54	21
2007	6277	3255	3022	92	21
Total	**30942**	**16033**	**14909**	**388**	**157**

Because congenital anomalies have effects on infant deaths, related indicators were calculated: mortinatality ratio, infant death rate and death rate due to congenital anomalies.

The prevalence of anomalies was 1.17% in live births. The prevalence of congenital anomalies for 2003-2007 period, was 1.22‰ in births. Birth rate increased from 8.3% in 2003 to 9.3% in 2007. Abortions had a maximum in 2003 (972.48‰ in live births) and a minimum in 2005 (598.648‰ in live births. Deaths caused by congenial anomalies increased during the studied period (Table 2).

Table 2. Demographic indicators between 2003-2007 in Cluj district

Year	Birth rate (%)	Mortinatality ratio	Infent death	Deaths by congenital anomalies (%)	Perinatal death (%)	New cases of congenital anomalies	Abortions (at 1000 live births)
2003	8.3	5.4	9.2	0.18	0.27	102	972.48
2004	8.8	3.8	12.9	0.37	0.38	79	681.5
2005	9.5	3.7	10.1	0.35	0.37	61	598.6
2006	9.8	3.8	9.1	0.28	0.31	54	615.2
2007	9.3	2.9	8.1	0.26	0.27	92	677.23

In the studied period was observed an increasing number of embryo-fetal malformations.

The distribution based on age groups at the diagnostic moment was different according to the expressivity and the severity of the clinical features: 40.46% in the first year of life, 27.06% between 1-14 years, 26.85% between 15-64 years and 5.7% over 65 years. The biggest number of cases is at the group under a year (Table 3).

Table 3. Congenital malformation distribution based on age groups at the diagnostic moment

Year	New cases of congenital anomalies	Group			
		< 1 year	**1-14 years**	**15-64 years**	**≥ 65 years**
2003	102	50	24	20	8
2004	79	34	19	22	4
2005	61	31	18	12	0
2006	54	21	12	17	4
2007	92	21	32	33	6
Total	**388**	**157 (40.46%)**	**105 (27.06%)**	**104 (26.8%)**	**22 (5.7%)**

The distribution based on residence environment reveals the fact that 63.4% of the cases are from urban area and 36.6% from rural area (Table 4).

Table 4. Congenital malformation distribution based on residence environment at the diagnostic moment

Year	Total	Urban	Rural	Ratio U:R
2003	102	54	48	1.125:1
2004	79	41	38	1.08:1
2005	61	33	28	1.18:1
2006	54	44	10	4.4:1
2007	92	74	18	4.11:1
Total	**388**	**246 (63.4%)**	**142 (36.6%)**	**1.73:1**

Regarding gender distribution, males have a bigger number (60.56%), according with literature. Details in Table 5.

Prevalence rate of congenital malformation was higher in males (1.46%: 235 live births malformation from 16033 live births) and lower in females (1.02%: 153 live births malformation from 14909 live births), and the difference between these was not statistically significant (p=0,0005 χ^2 test).

There are not statistically significant associations between the presence of congenital malformations and the residence environment.

Table 5. Congenital malformation distribution based on gender at the diagnostic moment

Year	Total	Male	Female	Ratio M:F
2003	102	62	40	1.55:1
2004	79	42	37	1.13:1
2005	61	37	24	1.54:1
2006	54	26	18	1.44:1
2007	92	68	34	2:1
total	**388**	**235**	**153**	**1.54**:1

The probable etiology of cases was established based on clinical examination, family medical history of illness, mother medical history and laboratory exams. From the total registered anomalies only 10.30% were chromosomal anomalies. For the rest of anomalies, only in one third of the cases maternal, environmental, socio-economic and educational etiological risk factors were determined:, mentioned in live births with anomalies registers (Figure 1).

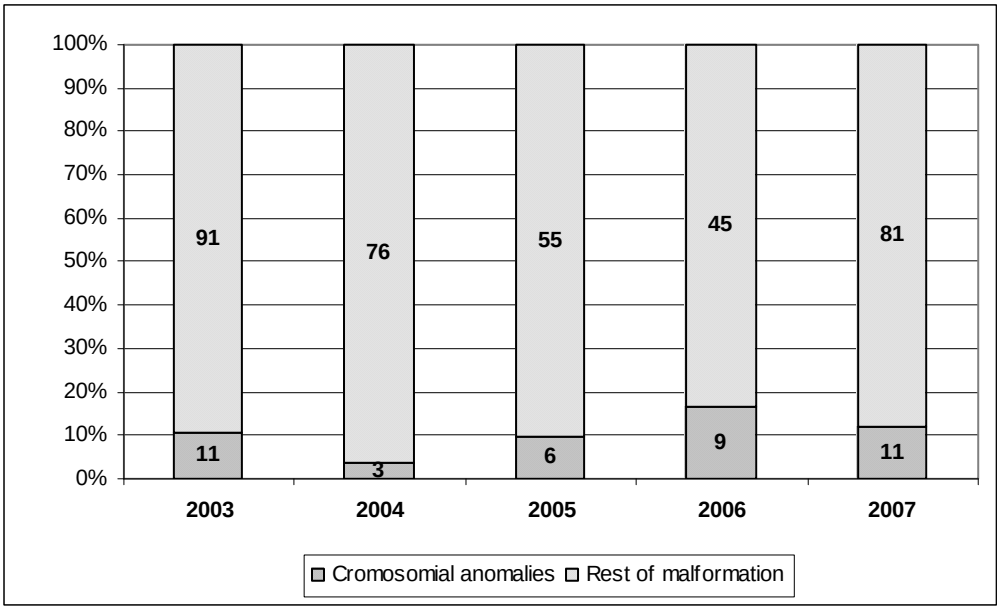

Figure 1. Chromosomal anomalies diagnosed in Cluj district in period 2003-2007

Mother medical history of illness was grouped in: viral infections, bacterial infections and other diseases (diabetes, thrombi embolic complications etc). The total was 116. From those, 92 (80%) have had a viral infection during the pregnancy, 20 (17%) had suffered a bacterial infection and (3%) had other diseases. Mother's medical history was present in the first trimester for 36 (31%) cases, in the second trimester for 45 (39%) cases, in the third trimester for 35 (30%) cases (Table 6).

Table 6. Mother pathologic history during pregnancy

Mothers	Trimester I	Trimester II	Trimester III	Total
Viral infection	32	34	26	92
Bacterial infection	4	9	7	20
Other diseases	0	2	2	4
Total	**36**	**45**	**35**	**116**

Some of the mothers with malformed children (5%) have had in their medical history: miscarriages, premature borne children, radiological investigations. None of them were vaccinated during pregnancy.

From all cases of major anomalies 90.72% were unique and the rest of them (9.28%) were with

multiple anomalies. The more frequent associations were for central nervous system anomalies and for oro-facial clefts.

The analysis of infant death causes between 2003-2007 indicated that the first causes of death were: perinatal illnesses (first place) and congenital malformations.

From all infant deaths, 42.95% are due to perinatal causes, 31.80% are due to congenital anomalies, and 15.40% are due to respiratory conditions. During 2003-2007, the death due to perinatal causes is decreasing, and the death due to malformations is constant (Table 7).

Table 7. Infant deaths causes in Cluj district during 2003-2007

Death causes	2003	2004	2005	2006	2007
Infectious and parasitic diseases	2	1	1	2	3
Respiratory diseases	13	15	5	6	8
Digestive diseases	0	0	1	1	0
Perinatal causes	22	31	31	26	21
Congenital anomalies	12	24	23	21	17
Accidents	2	2	1	1	1
Other causes	1	4	3	3	1
TOTAL	**52**	**77**	**65**	**60**	**51**

During 2003-2007, infant death caused due to congenital anomalies are localized in circulatory system (42.27%), digestive system (15.46%), nervous system (13.40%) (Table 8).

Table 8. Infant death due to congenital anomalies, in Cluj district, during 2003-2007

Infant deaths due to congenital anomalies	2003	2004	2005	2006	2007
Nervous system	2	4	4	3	0
Circulatory system	5	9	9	9	9
Respiratory system	1	0	0	0	0
Digestive system	2	3	5	2	3
Urinary system	0	1	0	0	0
Skeletal system	1	2	1	4	1
Other malformations	1	5	3	3	3
Other chromosomal anomalies	0	0	1	0	1
Total	**12**	**24**	**23**	**21**	**17**

Distribution Analysis of Congenital Malformations in ISP Cluj Territory

The dynamics for the new cases of congenital anomalies registered during 2003-2007 in the districts subordinated ISP Cluj is presented in Table 9.

Table 9. New cases of congenital anomalies in districts subordinated ISP Cluj during 2003-2007

District / year	2003	2004	2005	2006	2007
AB	7	3	14	9	7
BH	97	84	76	90	92
BN	2	5	3	1	2
CJ	102	79	61	54	92
CV	12	9	7	11	8
HR	17	19	21	18	10
MM	12	7	11	8	9
MS	88	81	64	52	87
SM	12	9	11	10	8
SJ	13	10	18	11	15
SB	29	21	23	26	31
Total	391	327	309	290	361

Repartition regarding residency environment revealed that 52.68% of the cases are from urban areas and 43.32% are from rural areas (Table 10).

Table 10. New cases of congenital malformation (residency environment) in districts subordinated ISP Cluj

District	Total district	Urban	Rural	U:R Ratio
AB	40	14	26	0.538:1
BH	439	235	204	1.152:1
BN	13	8	5	1.6:1
CJ	388	246	142	1.732:1
CV	47	12	35	0.343:1
HR	85	44	41	1.073:1
MM	47	27	20	1.35:1
MS	372	215	157	1.369:1
SM	50	23	27	0.852:1
SJ	67	23	44	0.523:1
SB	130	37	93	0.398:1
Total	**1678**	**884 (52.68%)**	**794 (47.32%)**	**1.113:1**

It was tested the association between residence environment and the appearance of congenital malformations in new born.

In the following districts: BN, CJ, HR, MM, SM, SJ there are not significant statistically differences due to the residence environment. In the following districts: AB, CV and SB these differences are statistically significant ($p < 0.05$) in the favour of rural environment; and in the following districts: BH, and MS, these differences are statistically significant ($p<0,05$) in the favour of urban environment.

During 2003-2007 in the 11 districts were registered 1087 deaths due to congenital malformations (Table 11).

Table 11. Deaths due to congenital malformations in districts subordinated ISP Cluj during 2003-2007

District / year	2003	2004	2005	2006	2007	Total
AB	23	25	20	16	16	**100**
BH	24	29	27	28	24	**132**
BN	44	19	22	23	22	**130**
CJ	15	30	29	23	20	**117**
CV	20	9	18	12	9	**68**
HR	14	9	13	12	12	**60**
MM	24	18	23	34	14	**113**
MS	35	19	27	21	22	**124**
SM	10	17	14	25	22	**88**
SJ	11	9	12	10	5	**47**
SB	15	26	23	15	29	**108**

Discussion

The prevalence at birth of congenital abnormalities can be defined as the number of newborns and premature infants with birth defects reported the total number of premature births and to a certain period of time in a given territory. We used prevalence instead of incidence at birth congenital abnormalities. to exclude the risk pregnancies which are completed either by miscarriage or by therapeutic abortion. Because of the incomplete records of the cases as "occult" anomalies were not included in the study. Early diagnosis of congenital malformations is a priority and should be taken care of by prenatal medicine given the special medical and also the social implications of a

malformed fetus. The diagnosis of certainty of malformations was obtained both clinically (hydrocephalus. oligoamnios) and laboratory (triple test results, TORCH, ultrasound and amniocentesis).

Diagnosed abnormalities were classified according to international classification code, version 10 (IDC-10).

Major structural anomalies were present at 39.51% (388 cases) of 982 patients which are in registered in Genetic Pathology Center from Pediatric Clinics I, Cluj, in period 2003-2007.

Diagnosed abnormalities included: congenital malformations of circulatory, respiratory, digestive, central nervous system, congenital malformations of skeletal system, Down syndrome, which is consistent with results of other studies showing that the most common are heart abnormalities (33.06%). followed in descending order of frequency by urinary. genital. CNS. skin. oral-facial cleft and digestive anomalies [1-7] .

Greater frequency of cardiac malformations is caused by the fact that many of cardiac defects escape in prenatal ultrasound diagnosis, being diagnosed post abortion or postnatal [8, 9]. Distribution of major structural anomalies, by gender (overall and by different types of abnormalities) was against male, with a ratio of M: F = 1.54:1, except genital system anomalies and skin anomalies that prevailed in females.

Major structural abnormalities had in descending order of frequency the following locations: cardiac (33.06%), bone (15.60%), urinary (13.22%), genital (11.37%), CNS (7.59%), skin (7.59%) oral-facial cleft (6.87%) and digestive (4.49%). In over 2/3 of cases the diagnosis was made within 6 months of life, of which in 1/2 of its first month. The present study is based on statistical and clinical data of malformed children and information on maternal history shows the risk of maternal exposure to potentially teratogenic conditions. A group of mothers who have a high risk of giving birth to a newborn with deficiencies could be defined by: previous abortions, maternal age, acute viral and bacterial infections during pregnancy. Some mother's illnesses may increase the risk of congenital anomalies. According to some authors, diabetes, hypertension and hypothyroidism are associated with congenital anomalies [10].

In this study diabetes was the only maternal disease that was associated with congenital anomalies. According to some authors, diabetes may result in embriopathy with malformations or miscarriages in first trimester of pregnancy [11].

We can not conclude which of these factors may be the cause, or may reflect adverse consequences of abnormal development, but we can say, perhaps, that there was a combined effect of these factors added up.

10.30% of the chromosomal abnormalities, mothers acknowledged the presence of genetic family history with the presence of the genetic disorders. At more than 35 years, there is an increased risk of malformed children, probably due to disturbed maternal-fetal exchange in the endometrium. Higher rate of malformations in this category could be explained on the one hand due to a more frequent screening of the patients aged over 31 years, and on the other hand due to maturity and different medical education of these patients . All these factors are recognized in many clinical-laboratory studies as the most important factors involved in the embryo pathogenesis of malformations [5, 9, 12-14].

It 27% of the cases of the mothers with a history of gynecological repeated miscarriages or premature births, the causes could be both genetically factors and local gynecologic factors. Some studies confirm this finding [15, 16]. Interestingly, some mothers said they experienced in different periods of pregnancy acute viral infectious and bacterial diseases.

The study focused on viral and bacterial infectious diseases experienced by the mother in different periods of pregnancy. The completion of survey sheets of malformed children has faced some problems, including record hiatus regarding any problems occurred in pregnancy and possible sub clinical infections that might affect the course of pregnancy, but they have gone unnoticed by pregnant women. Regarding the etiology, in 1/3 of cases were identified etiological risk factors. Of all mothers of malformed children, 92 had a viral infection during pregnancy and 20 bacterial infections. TORCH complex performed in pregnant women to control presentation highlighted passage through one or more infections.

Recorded congenital abnormalities were well defined and coded, but they do not cover all the anomalies in a population like that of a district. a number of cases presenting some malformations

that were not detected or were neglected because of the patients' personal reasons that not have made prenatal advice.

This difference between districts was due to various screening and antenatal diagnosis possibilities and to the termination of pregnancy as an option when the anomaly had been diagnosed prenatal [17].

It is to be noted that the study included cases diagnosed at birth and classified according to IDC-10. In this study the rate of congenital abnormalities was higher at the female gender than at the male gender and the difference was statistically significant.

The finding is at odds with some studies that found no correlation between gender and the rate of abnormalities [18]. On the other hand it is supported by a study conducted in Iran, which showed in turn a higher rate of abnormalities in male newborns [19].

We expected not to find an interrelation between the rate of congenital abnormalities and environment of origin of cases, the differences are not statistically significant in some districts. However, in other districts (AB. BH. CV. MS and SB) rates of congenital malformations showed statistically significant differences between urban and rural areas. We found that no studies have obtained these results, so this result will be the subject of future studies.

Congenital malformations have gained importance due to mortality and morbidity [20-22]. According to some authors, the chance of a child with birth defects to die in neonatal period is 3.85 times higher and 2.81 times higher in the post-neonatal period compared with children without birth defects. Congenital malformations have the same magnitude in determining perinatal mortality [23].

Between 2003-2007 the main causes of death among 0-1 year age group were diseases of perinatal period, followed by congenital malformations. The most common anomalies were those of cardiovascular followed by bone, urinary and genital abnormalities.

The birth of a child with minor or major structural birth defects implies many medical and aesthetic problems, their treatment being the result of many medical professionals as well as psycho-social, which attests the importance of prophylaxis [24]. Most children born with major congenital abnormalities that survive are affected physically, mentally or socially and may represent an increased risk of morbidity due to defects that you have.

Regarding prophylaxis, although progress in this area is amazing, there is still a significant percentage of cases of fetal abnormalities that are beyond the prenatal diagnosis. For this reason, one that deals with prenatal diagnosis should be aware of the heavy responsibility assumed. in the first place to patient, represented by the fetus, but also to his family and not least to society [15, 16, 25].

Prenatal diagnosis has some advantages, in the first place, allowing optimization of therapeutic indications on therapeutic abortion in congenital and hereditary diseases and improving the serious negative psychological impact, which has on the couple's parental birth of a malformed child. through its information even during pregnancy. Although screening laboratory facilities are becoming more efficient, embryo malformations are actually increasing.

Conclusions

The most common major structural abnormalities are those with cardiac localization, followed by bone, urinary and genital abnormalities.

During the time studied, the prevalence of congenital abnormalities increased and at the same time, increased deaths due to them.

During 2003-2007 congenital abnormalities were ranked on the second place as a cause of death being preceded by perinatal causes and succeeded by respiratory pathology.

In terms of the structure of deaths per age group under one year, deaths were due to circulatory abnormalities, followed by those of the digestive system and CNS.

On the geographical territory studied, there was a geographical variation in the number of cases, the maximum being in the district Cluj and minimal in the Sălaj district.

Regarding gender distribution of major structural abnormalities, the one most affected is male.

Only in certain geographical areas were statistically significant differences between the prevalence rate of congenital malformations in urban and rural areas.

In the study a clear annual growth in the number of embryo-fetal malformations was observed, most likely due to optimizing resources prenatal investigation.

The etiology of most birth defects is not known enough, however, some factors are well known and they form the basis for screening and prevention interventions.

Early diagnosis of congenital malformations is a priority for prenatal medicine, certainty diagnosis being both clinical and laboratory.

Although there is great progress made in prevention, there is still a significant percentage of cases of fetal abnormalities that escapes prenatal diagnosis.

Prenatal diagnosis allows both optimization of therapeutic opportunities and improving the negative psychological impact that it the birth of a malformed child has.

Because of the particular impact of congenital malformations on public health, interest in determining the causes and development, implementation and evaluation of prevention programs is growing.

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