Congenital Anomalies in the Pediatric Population of the Republic of Moldova: A Retrospective and Descriptive Study

Buta Galina
"Nicolae Testemitanu" State University of Medicine and Pharmacy of Moldova,
The National Center for Public Health
butagalina@yahoo.com
Russu-Deleu Raisa
"Nicolae Testemitanu State" University of Medicine and Pharmacy of Moldova
raisa.russu@usmf.md

Abstract

This paper presents the results of a retrospective analysis of congenital anomalies (CA) in the Republic of Moldova (RM) over a period of 11 years (2004-2014). The spread of CA in Moldova during the analyzed period is characterized by a stable level. In the infant mortality structure, congenital anomalies ranked second. There is a significant increase in CA, caused by chromosomal and cardiovascular system anomalies, with an average annual rate of 0.1 and 0.5%, respectively. At the same time, the CA of the musculoskeletal system has a reduction trend with a average annual rate of -2.7%. Stabilization of CA spread is the result of the implementation of the national program for the prevention and reduction of mortality and morbidity in children with congenital anomalies and hereditary diseases for the years 2013-2017. Some identified trends demonstrate the existence of gaps in the primary health care work concerning family planning.

Key words: congenital anomalies, disease dynamics, infant mortality
J.E.L. Classification: I15

1. Introduction

Congenital malformations/anomalies are part of the *disease* category which for decades has attracted the attention of the scientific community and public health because:

- They relate to the most serious deviations in children's health and significantly influence child mortality, morbidity and disability (EUROCAT Website Database, 2010; EUROCAT Working Group, 1997; Демикова, 2003);
- They are common among human populations, representing a significant part of the genetic burden (Boyd et al., 2011; Dolk et al., 2011; Knowles et al., 2012; Гинтер, Зинченко, 2006);
- The frequency of congenital malformations in people, according to WHO experts, ranges according to the country from 2.7% up to 16.3%, with an average of 5% (Corsello, Giuffrè, 2012; Информационный бюллетень, 2012);
- They constitute the 5th cause of death in the first 4 weeks from birth (Archer et al., 2011; Hotarârea Guvernului R.M. No. 988/06.12.2013).
- Significant economic costs are needed to provide high-quality medical and social assistance to children with disabilities, including pedagogic correction of defects and long-term symptomatic treatment for patients with congenital anomalies (EUROCAT Working Group, 1997; EUROCAT, 2005, Hotarârea Guvernului R.M. No. 988/06.12.20135; Демикова, 2003). Patients with such pathology occupy approximately 30% of the beds in childcare facilities for children of all profiles (Calzolari et al., 2004; Hotarârea Guvernului R.M. No. 988/06.12.2013).

- the moral and psychological aspects of the impact of the birth of a child with congenital anomalies on the well-being of families and society as a whole are also very significant (Демикова, 2003).
- WHO attributes congenital anomalies to the pathology-indicator category, reflecting the high degree of environmental dependence (Информационный бюллетень, 2014).

At the same time, the actual frequency of congenital anomalies remains imprecise, due to diagnostic difficulties and various approaches to registration (Knowles et al., 2012; Информационный бюллетень, 2014). To implement effective and appropriate measures to reduce the prevalence of congenital anomalies, it is necessary to know (become aware of) several important parameters. First of all, it is necessary to have information on the frequency of congenital anomalies. Secondly, there is a need for information on the structure of developmental defects, because any anomaly is heterogeneous in terms of clinical manifestations. Thirdly, it is important to know which factors induce the development of malformations. In order to control these parameters it is necessary to perform complex epidemiological studies of congenital malformations, involving primary medicine and the public health surveillance service.

2. Case Study

In view of the above, it is of scientific interest that the retrospective and prospective analysis of the morbidity by congenital anomalies in the Republic of Moldova recorded over a sufficiently long period to be performed.

Aim of the study: To identify the particularities concerning the spread, structure and dynamics of congenital anomalies in RM correlated with the management of toxic wastes from industrial activities.

Materials and methods

The study includes the retrospective analysis of morbidity and mortality by congenital malformations of children aged 0-17, 11 months and 29 days from the Republic of Moldova, based on the statistical reports existing at the National Center for Health Management. The observation period covers the years 2004-2014.

The frequency of different types of congenital malformations was analyzed on segments, organs and systems according to CIM, WHO's Xth revision, their spread and dynamics being compared with the administrative-territorial units.

The analysis of the spread of toxic industrial waste (TIW) was carried out according to the data from the National Bureau of Statistics database, available on www.statistica.md., and on the basis of the statistical report F-1/e "Formation, Use and Neutralization of Toxic Waste", existing at the level of the Occupational Health Care Section of CSP Chișinău Municipality.

In the analysis of the chronological series, the absolute increase with fixed base and mobile base, the rhythm of variation, the growth rate, the index of visibility (demonstration index), the absolute value of 1% growth were calculated. In addition, for the sake of clarity, the interval consolidation (Jaba, 1998; Сепетлиев, 1968) was also used.

3. Results and Discussions

In the period 2004-2014, 429699 children were born in the Republic of Moldova, out of which 426926 (99.35%) were born alive and 2773 (0.65%) were born dead. During that time there were 70487 cases of congenital anomalies among children, which represents an average of 786.4 ± 29.45 cases per year. The frequency of congenital anomalies in the population was 22.35 ‰.

During the observation period, the infant mortality due to congenital malformations remains constantly increased, ranging from 2.6 to 3.9 cases per 1,000 live newborns, being more pronounced in the 0-4 year age segment, on the background of the downward trend, at a rate of -2.1% annually at the level of infant mortality and at a rate of -2.6% in the mortality rate of children aged 0-4 years.

Congenital anomalies rank second in the infant mortality structure, being 29.8 ± 0.71% in infant mortality and 27.6 ± 0.68% in mortality rates for children aged 0-4 years, with a fluctuation range within 24.8 and 36.7%.

In terms of morbidity indices, the downward trend of incidence with the annual average rate of -0.8% and the upward trend of prevalence, with the annual average rate of + 1.7% (Table 1) are attested.

Table no. 1. Dynamics of Congenital Anomalies in Pediatric Population of the Republic of Moldova during 2004-2014

Years	Items	Absolute growth		Visibility index, %	Variation rate, %	Absolute value of 1% growth	Interval consolidation method	Mobile average method
		With fixed basis	With mobile basis					
Incidnce, cases in 10 thousand people								
2004	18,94	-	-	100	-			
2005	21,83	2,89	2,89	115,3	15,3	1,18	20,39	20,50
2006	20,45	1,51	-1,38	93,7	-6,3	2,63		21,00
2007	16,19	-2,75	-4,26	79,2	-20,8	0,59	18,32	18,00
2008	15,47	-3,47	-0,72	95,6	-4,4	2,63		16,00
2009	15,01	-3,93	-0,46	97,0	-3,0	3,70	15,24	15,00
2010	18,52	-0,42	3,51	123,4	23,4	0,63		17,00
2011	18,29	-0,65	-0,23	98,8	-1,2	11,99	18,41	18,20
2012	18,79	-0,15	0,5	102,7	2,7	5,45		18,50
2013	17,4	-1,54	-1,39	92,6	-7,4	1,82	18,10	18,00
2014	16,38	-2,56	-1,02	94,1	-5,9	2,12		17,00
Prevalence, cases in 10 thousand people								
2004	58,11	-	-	100	-			
2005	62,6	4,49	4,49	107,7	7,7	0,58	60,36	60,0
2006	62,1	3,99	-0,5	99,2	-0,8	4,99		62,0
2007	58,56	0,45	-3,54	94,3	-5,7	0,08	60,33	60,0
2008	58,42	0,31	-0,14	99,8	-0,2	1,55		58,0
2009	55,38	-2,73	-3,04	94,8	-5,2	0,53	56,90	58,5
2010	63,12	5,01	7,74	114,0	14,0	0,36		58,0
2011	64,68	6,57	1,56	102,5	2,5	2,66	63,90	64,0
2012	68,14	10,03	3,46	105,3	5,3	1,87		66,0
2013	68,33	10,22	0,19	100,3	0,3	36,65	68,24	68,0
2014	67,78	9,67	-0,55	99,2	-0,8	12,09		68,0

The rate of variation in the incidence of malformations relative to the main causes has statistically significant differences ($p < 0.01$). Thus, the tendency for growth is characteristic of congenital anomalies due to chromosomal deformations and abnormalities of the circulatory apparatus with the corresponding average annual rate of 0.1% and 0.5%, respectively. At the same time, malformations and deformities of the osteo-muscular system exhibit a diminishing tendency, with an average annual rate of -2.7%.

The increasing trend of congenital anomalies through chromosomal and circulatory system abnormalities and disturbances is assessed as an unfavorable prognosis for the future, requiring the implementation of urgent (prompt) measures to stabilize the process and conducting epidemiological studies for a deeper analysis of the situation and for finding efficient measures for prevention and control.

Throughout the observation period, the proportion of birth defects in the overall incidence in newborns is significantly higher among preterm infants compared to those born in the term - 15.6 ± 1.53% vs. 5.5 ± 0.47%, respectively. This reveals a significant difference of about 3 times ($p < 0.05$), which is in full accord with the references of the specialized literature.

The structure of morbidity through congenital anomalies in the pediatric population of the Republic of Moldova is dominated by multiple malformations that account for almost one-quarter of all recorded malformations (Table 2). The second rank in the structure are the anomalies of the

osteo-articular system, although the registered proportions show a decreasing tendency (21.2 - 19.1%). In the third position are the malformations of the circulatory system, but the proportions recorded are increasing continuously.

Table no. 2. The structure of morbidity through congenital anomalies in the pediatric population of the Republic of Moldova; Average data for the period 2004-2014

	Types of congenital anomalies	Code CIM-10	RM		Rank
			%	±Δ%	
1	Congenital anomalies of the nervous system	Q00 - Q07	11,9	4,63	IV
3	Congenital anomalies of the circulatory system	Q20 - Q28	15,2	1,03	III
4	Congenital anomalies of the respiratory system	Q30 - Q34			
5	Congenital anomalies of the gastrointestinal tract	Q35 - Q45	7,4	3,25	V
7	Congenital urinary system	Q60 - Q64	6,9	3,42	VI
8	Congenital anomalies of the musculoskeletal system	Q65 - Q79	19,8	2,45	II
10	Other multiple congenital anomalies	Q86 - Q89	25,3	0,84	I

The comparative analysis of the spread of congenital anomalies along the territorial profile reveals reporting variations in the territorial-administrative units at *quintile* levels. Due to lack of space, we considered it appropriate to only present the data about the congenital malformations of the circulatory system, as they have the highest rate of variation. Thus, in the last year compared with the first year of the study, the status quo is attested in 10 districts (Donduseni, Riscani Floresti, Falesti, Telenesti, Soldanesti, Anenii-Noi, Cimislia, Ialoveni, Cahul), an upward trend in 14 districts (Rezina, Orhei, Straseni, Criuleni, Leova, UTAG, Edinet, Glodeni, Calarasi Dubasari, Cantemir, Briceni, Chisinau and Nisporeni) and a downward trend in 9 districts (Hincesti, Stefan-Voda, Ocnita, Drochia, Soroca, Siingerei, Balti Taraclia, Causeni) (Table 3.).

Table no.3. The dynamics of the congenital anomalies of the circulatory system from the territorial perspective, in relation to "quintiles" (districts)

Qiuntila		2004	2014
V	Up the hill	Falesti, Floresti, Telenesti, Hincesti, Basarabeasca, Stefan-Voda	Falesti, Floresti, Telenesti, Rezina, Orhei, Straseni, Criuleni, Leova, UTAG, Basarabeasca
VI		Balti, Singerei, Orhei, Strasani, Criuleni UTGA, Taraclia	Edinet, Glodeni, Calarasi, Dubasari, Hincesti,Cantemir, Stefan-Voda
III		Ocnita, Edinet, Donduseni, Drochia, Soroca, Rezina, Criuleni, Cimislia, Leova, Anenii-Noi	Briceni, Donduseni, Chisinau, Anenii-Noi, Cimislia
II		Glodeni, Ungheni, Chisinau, Dubasari, Calarasi, Causeni, Soldanesti	Ocnita, Drochia, Soroca, Soldanesti,Singerei, Balti, Ungheni, Nisporeni
I	Down the hill	Briceni, Râscani, Nisporeni, Ialoveni, Cantemir, Cahul	Ialoveni, Cahul, Taraclia, Riscani, Causeni

Starting from the fact that WHO considers congenital malformations as a pathology-indicator of ecological status, we considered it important to correlate the intensity of CA with toxic industrial waste (TIW). During the period analyzed in the Republic of Moldova, 1.0 ± 0.16 thousand tons of TIW was formed, which represents 0.42-0.50% of the volume of production and consumption

waste. At the same time, however, it should be noted that practically the number of industrial waste-producing enterprises, increased by 30%, from 630 units in 2001 to 978 units in 2014, which demonstrates the spread of this phenomenon as well as an uneven level in the country (Table 4).

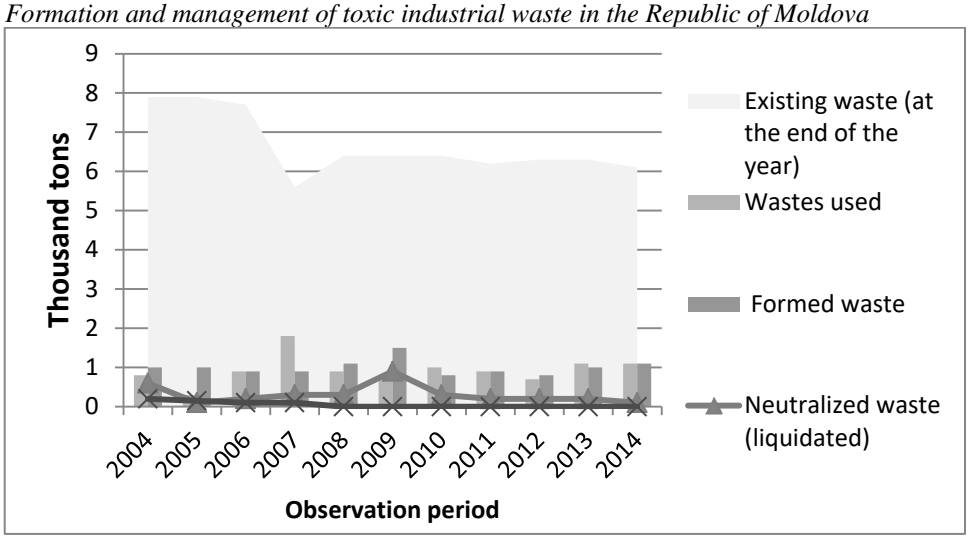
Table no. 4. Evolution of toxic industrial waste in RM by regions: Average data between 2004 and2014

No.		Formed during the year		Existing at the end of the year	
		thousand tons	**%**	**thousand tons**	**%**
1	RM	2338,9±214,34	100,0	6539,1±63,60	100,0
2	Chisinau Mun.	443,8±125,79	18,9±4,85	443,8±125,79	33,4±1,16
3	North	793,9±39,90	35,2±,79	610,5±4,46	9,8±0,14
4	Balti Mun.	125,0±16,07	5,7±0,99	589,8±5,65	9,5±0,15
5	Centre	688,7±171,08	28,2±3,98	1481,4±34,34	23,3±0,40
6	South	372,6±122,24	32,2±1,12	2042,3±82,15	27,0±32,15
7	U.T.A. Gagauzia	39,9±7,65	2,0±0,36	88,5±4,65	1,4±0,07
P_{3-5}		<0,05		<0,05	
P_{3-6}		<0,05		<0,05	
P_{5-6}		<0,05		<0,05	
P_{3-7}		<0,05		<0,05	
P_{2-5}		<0,05		<0,05	
P_{3-4}		<0,05		<0,05	

In Balti municipality, there were more TIW compared to Chisinau - 589.8 ± 5.65 tons versus 443.8 ± 125.79 tons (Table 4). At the same time, the cumulation of TIW assessed by the volume of existing waste at the end of the year, shows that in Chisinau there is one third of the TIW accumulated in RM - 2120.0 thousand tons out of 6352.1 thousand tons, which is negative from the public health point of view, including the incidence of CA.

It should be mentioned that the amount of toxic industrial waste at the end of the year in relation to the volume of waste formed in the environment during the observation period is 9.5 ± 0.99, i.e. practically 10 times higher (fig.1).

Figure 1. Formation and management of toxic industrial waste in the Republic of Moldova



In the North region, 5 districts (Briceni, Falesti, Floresti, Riscani, Singerei), according to official statistics, are free of TIW. The largest amount of TIW is accumulated in Donduseni (11.9 ± 1.71 tons) and Soroca (2.1 ± 0.44 tons) in the North region (*raioane*).

In the Central area, 3 districts are free from TIW (Dubasari, Rezina, Șoldanesti) and the leading holders are Ialoveni (576.1 ± 45.91 tons), Orhei (368.6 ± 4.01 tons), Calarasi (180,4 ± 18.90 tons) regions (*raioane*). In Hincesti and Telenesti districts, the accumulated TIW volume is practically at the same level, i.e. 101-107 tons.

In the South Zone, the regions of Cantemir and Ștefan-Voda are free of TIW, and the leaders in the accumulation process are Causeni (1140.8 ± 26.57 tons), Taraclia (348.9 ± 26.57 tons), Leova (229.7 ± 5.59 tons) and Cahul (218.2 ± 0.22 tons) regions.

Therefore, there is a correspondence of 87.3% between the accumulated TIW volume in the top *quintile* (district) and the incidence of congenital anomalies.

4. Conclusions

Our conclusions are as follows:

1. Population prevalence of congenital anomalies in the Republic of Moldova remains constantly high - 22.35 ‰.
2. During the 11-year period under observation, the incidence of congenital anomalies was characterized by a tendency to decrease, mainly due to the number of osteo-muscular system anomalies.
3. DTI represents a major risk to the health of pediatric population and requires extensive epidemiological studies on CA in relation to environmental factors.
4. To make prevention and control measures more effective, inter-sectoral and interdisciplinary measures promoted at the policy level are needed.

5. References

- Archer J.M., Yeager S.B., Kenny M.J. Distribution of and Mortality from Serious Congenital Heart Disease in Very Low Birth Weight Infants // Pediatrics. - 2011. - V. 127. № 2. - pp. 293-299.
- Boyd P.A., Tonks A.M., Rankin J. BINOCAR Working Group. Monitoring the prenatal detection of structural fetal congenital anomalies in England and Wales: register-based study // J. Med. Screen. - 2011. - V. 18, № 1. - pp. 2-7.
- Calzolari E., Bianchi F., Rubini M. Epidemiology of cleft palate in Europe: implications for genetic research // Cleft Palate Craniofac J. - 2004. - V. 41. - pp. 244-249.
- Corsello G., Giuffrè M., Prematurity and twinning. //The Journal of Maternal-Fetal & Neonatal Medicine. 2012. Volume 25, - Issue sup3. Pages 6-10 | Published online: 28 Sep 2012 [Online] Available at: http://dx.doi.org/10.3109/14767058.2012.712350 [Accessed 27 March 2017]
- Демикова Н.С. Мониторинг врожденных пороков развития и его значение в изучении их эпидемиологии // Российский вестник перинатологии и педиатрии. - 2003. № 4. - С. 13-17.
- Dolk H., Loane M., Garne E. Congenital Heart Defects in Europe Prevalence and Perinatal Mortality, 2000 to 2005 // Circulation. - 2011. - V. 123. - pp. 841-849
- EUROCAT Website Database. [Online] Available at: http://www.eurocat.ulster.ac.uk / University of Ulster, 2010 [Accessed 27 March 2017].
- EUROCAT Working Group (1997) Eurocat report 7. 15 years of surveillance of congenital anomalies in Europe 1980-1994. // Scientific Institute of Public HealthLouis Pasteur. Brussels.
- EUROCAT. Instructions for the Registration and Surveillance of Congenital Anomalies. 2005. [Online] Available at: http://www.eurocat.ulster.ac.uk/pubdata [Accessed 27 March 2017]
- EUROCAT. [Online] Available at: http://www.eurocat-network.eu/
- Гинтер Е.К., Зинченко Р.А. Наследственные болезни в российских популяциях // Вестник ВОГиС. - 2006. Т. 1. № 1. - с. 106-125.
- HOTARIREA GUVERNULUI RM, Nr. 988 din 06.12.2013 Cu privire la aprobarea Programului naţional de prevenire şi reducere a mortalităţii şi morbiTIWaţii copiilor prin malformaţii congenitale şi patologii ereTIWare pentru anii 2013-2017. Publicat: 13.12.2013 in Monitorul Oficial Nr. 291-296 art Nr: 1097 [Online] Available at: http://lex.justice.md/index.php?action=view&view=doc⟨=1&id=350701 [Accessed 27 March 2017]
- Информационный бюллетень ВОЗ, 2012 г.
- Информационный бюллетень ВОЗ, 2014 г.
- Jaba E. Statistica. Bucuresti: ETIWura Economica. 1998.

- Knowles R.L., Bull C., Wren C., Dezateux C. Mortality with congenital heart defects in England and Wales, 1959-2009: Exploring technological change through period and birth cohort analysis // Arch. Dis. Child. - 2012. - V. 97. № 10. - pp. 861- 865.
- Kurinczuk J.J., Hollowell J., Boyd P.A. Inequalities in infant mortality project briefing paper 4. The contribution of congenital anomalies to infant mortality. Oxford: National Perinatal Epidemiology Unit, 2010. [Online] Available at: www.npeu.ox.ac.uk/infant-mortality [Accessed 27 March 2017]
- Сепетлиев Д. Статистические методы в медицинских научных исследованиях. Авторизированный перевод с болгарского языка. Москва: Медицина.1968. 418 с.