Newborns and intellectual disability: The Czech case *

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Down's syndrome is the most common genetic cause of intellectual disability (ICD-10, dg. Q90). Within the context of reproductive changes in practically all developed populations due to delayed childbearing, the consequences of newborns with Down's syndrome is a serious research topic. Several factors are related to the rate of Down's syndrome and its prevention. In countries where medical terminations of pregnancy are legal, these factors range from ethical and moral to economic considerations; parental preferences and professional attitudes (rooted conventions frequently persist over many decades) to economic sense (effort to reduce „the cost of life-long" care).

Since 1959 when French genetic Jerome Lejuene found that individuals with Down's syndrome possessed additional genetic material in their cells, usually an extra chromosome, medical research has been fully concentrated into the prenatal period. With extensive progression in the use of prenatal diagnosis techniques, the impact of selective termination creates "new structural" disparities in the newborn/parental cohorts, exactly in countries where elective abortion are performed (e.g. Kuppermann, 1996; Khoshnood, 2000 and 2004).

The goal of this Czech case study was to improve the overall knowledge and clinical practice related to the increase in the number of older women having children, and its consequences for children born with congenital intellectual disability caused by genetics. The first stage of evaluation was concentrated on prenatal time and on selective terminations of affected pregnancies with DS. The second stage was oriented toward postnatal period and on disparities in the birth prevalence of DS.

Materials and Methods

For the prenatal period we used data from the Congenital Malformations Monitoring Programme[1] for the period 1994 to 1998. Our study included 344 cases of pregnancy terminations of Down's syndrome that were due to the mother's age.

A specific cohort data set was created for studying processes in the postnatal period – during the first year of life. A total of 475 834 infants (live births=474 314 and stillbirths=1520) in the Czech Republic from 1994-98 were matched with congenital anomalies records from 1994-99, and infant death records from 1994-99. The linked congenital anomaly file contains 11 528 records. The death file contains 3 037 records. The number of newborns with Down's syndrome was 251. Survival of children with Down's syndrome during the first year of life was studied. The probability of survival at one year of age was analyzed for mortality timing.

The cohort file comprised all newborns born in the Czech Republic during five years. The use of the data was in accordance with the statutory obligations to protect confidentiality. Individuals could not be identified from the data provided for analysis. We present here the results of the age-adjusted analyses by logistic regression models. The analyses were carried out using the SPSS (SPSS Inc, Chicago, USA) statistical packages.

Results

Prenatal time: Table 1 shows the distribution of 595 cases of pregnancies with Down's syndrome (344+2+249) according to maternal age in the study period 1994-1998 in the Czech Republic. Overall prevalence rates of pregnancies with DS was 12,5 per 10 000 births, representing 1 case of DS for every 800 pregnancies (this does not include cases of spontaneous abortions for which we do not have data). The majority of these pregnancies (58%) was ended before birth by induced abortion (7,23 per 10 000 births). The highest number of pregnancy terminations for DS – 80 cases -- had mothers at the age group 35-39 years, constituting almost 20% of pregnancy terminations (rates 42 per 10 000 births). The rest of the affected pregnancies (42 per cent) were brought to term (249 newborns with DS live births and 2 stillbirths).

[1] A registration of congenital malformations began in the Czech Republic in 1961 and regular monitoring started in 1975. The Programme was a founding member of the International Clearinghouse for Birth defects Monitoring System (ICBDMS) and is a full member.

Postnatal time: The crude observed birth prevalence of Down's syndrome in Czech Republic was 5,27 per 10,000 births. This figure represents 1 case of Down's syndrome for every 1,900 live births. The largest proportion of newborns and newborns with Down's syndrome was among mothers aged 20-24 years. The birth prevalence rates of Down's syndrome substantially increased with increasing maternal age, with the maternal age group above 45 years constituting more than 250 per 10,000 births (Table 1). There is a large difference in the proportion of Down's syndrome babies born to younger women (< 35 years). This group comprised 87.3% of Down's syndrome babies. The mean maternal age (SD) was 25.1 (4.9) years for mothers of all children and 26.9 (6.3) years for mothers of children with Down's syndrome. The maternal age difference between non-Down's syndrome and Down's syndrome children was significant ($t = 6.11$, $p<0.001$).

Table 2 shows the results of the logistic regression analyses of the birth cohort study of the differences in the birth odds of Down's syndrome. Crude (OR) and fully adjusted odds (adj. OR) ratios for birth prevalence of Down's syndrome by birth order, education of mothers, and maternal age for the study population was calculated. The odd ratio of Down's syndrome for birth order was higher for women with three and higher birth order, crude OR – 1,82; 95% CI, 1,33-2,48 (with comparison with reference category first birth order). This difference appeared after adjustment for the mother's age, too. After simultaneously controlling for 3 covariates, the effects of birth order and maternal education was not significant. Only the effect of a mother's age on birth prevalence of Down syndrome was clear. From the age group 30-34 the odds ratio significantly increased. For example, a mother within the age group 30-34 years had 2,09-fold increase (adjusted OR – 2,09 with 95% confidence interval in 1,11-3,95), a mother within the 35-39 years age group had 2,81-fold increase (adjusted OR – 2,81; 95% CI, 1,36-5,80) in the odds of a birth with Down's syndrome as compared with mothers in the youngest age groups (below 19 years).

In the study birth cohort (475 834 newborns), 99,4% of them survived one year, while babies born with birth defects comprised just under 91,5 % which is consistent with the value of infant mortality quotients (0,64 and 8,46 per 100 live born infants). Within the group of newborns with Down's syndrome, 84,7% survived one year and infant mortality quotients for this sub-group was 15,3 per 100 live born infants; limits factors are congenital heart defects (CHD). During the first year of life in this cohort, 3037 children die, including one half before the age of 10 days, and 75% before the age of 64 days.

Discussion

Very low live birth prevalence rate of Down's syndrome (5.3 cases per 10,000 newborn infants) and a low proportion of children with Down's syndrome born to women after 35-years of age (about 13%) supports consistent detection of this type of birth defect during pregnancy (almost 1 from 6 newborns had invasive diagnostic testing procedures during pregnancy, for example in 2003 14,984 from 93,185 newborns had diagnostic test) and a high ratio of terminated pregnancies. That we found no significant differences in the prevalence of Down's syndrome by maternal education for the Czech population is consistent with the fact that prenatal care is offered free and on the same qualitative level to all women (Dzurova and Pikhart, in press).

Czech heath care, especially care for infants and mother, has been of very high quality for a long time (e.g. very low infant and maternal mortality, practically all deliveries are in maternity hospitals). The proclaimed health reproductive policy is to provide the best care for all on the same quality in order to obtain the high "quality" of newborns. Elective abortion has been generally accepted as the best solution for birth defects. In terms of the relationship to its socialist past, when conditions were relatively egalitarian and health care was free (Rychtarikova, 2001), contemporary global social changes might very well play a significant role in widening the social gap not only in health care, but also in care for infants.

More information for the explanation of "Down's syndrome mother prenatal behavior" is possible to add from the ***international perspective***. In the study year (1998), 14 programs in the world provided data on 1 809 cases of Down syndrome, of which 936 of them (51,7%) were terminated before birth. The percentage of terminations for DS ranged from the lowest value in the province of Alberta, Canada (25,8%), where the majority of affected pregnancies were brought to term, to the highest in France, in Strasbourg[2] (88,9%) and Paris[3] (74,5%) (ICBDMS, 2000), where conversely a large majority of these pregnancies were interrupted. The Czech Republic data showed that a value around sixty percent was a little bit higher that the average level (51,7%), Table 3.

[2] Around Strasbourg and the Bas-Rhine (area covered about 2% of all births in France).
[3] Area covers population of Greater Paris (representing 5% of the births in France).

The prevalence rate of Down's syndrome relates to ***prenatal screening techniques*** and techniques for definitive prenatal diagnosis. Recently, prenatal diagnostics of DS in the Czech Republic is based on second trimester screening methods – both biochemical and ultrasound ones. The efficiency of DS prenatal diagnostics is around 66 – 67 % in 2004, which is, most probably, a maximum value for these methods. In order to increase the prenatal screening efficiency and to move the diagnostics towards earlier stages of pregnancy, methods of first trimester screening are gradually being introduced. At present, first trimester screening is already available at some prenatal diagnostics department and it is expected to be implemented at other departments as well.

There were also large regional disparities in international comparisons in terms of the proportion of pregnancies with DS which were terminated among women at higher risk (35 years old and above) - almost 85% in the Czech Republic, 78% in France, Paris district. The lowest percentages of induced abortion were observed in Canada, the province of Alberta (44%) (Table 3). The most common medical technology of prenatal diagnosis in 1998 was amniocentesis (AC), with a mean level 77%; next was Chorion villus sampling (CVS) with 18,4%, and a few used Cordocentesis (CC), less than 5% (in 14 monitoring programme ICBDMS, 2000). Chorion villus sampling was more used in the province of Alberta, and Cordocentesis in the Czech Republic (Table 4). According ICBDMS, the population disparities in selective termination for DS reflects mainly the level of diffusion of the medical technology of routine prenatal screening, the strategy of prevention for DS, and the national regulations in the case of the late diagnosis, for example in France where there is no upper time limit for pregnancy termination (ICBDMS, 2000).

It is clearly recognized that prenatal screening for Down's syndrome is driven by several primary forces: the effort to reduce ''the costs of life-long care'' for people with Down's syndrome through medical technology; clinical support for individual choices of mothers or couples; and public health strategies designed to reduce birth defects and improve reproductive outcomes (Alderson, 2001). The social benefits of prenatal screening of Down's syndrome are very important. When a pregnancy with Down's syndrome continues, the main goal is to support socially disadvantaged families, and to help to start lives of children born with Down's syndrome. Relatively low infant mortality of children with DS (15.3 cases per 10,000 live born infants) can be understood by the following factors: (i) medical technology development, such as better surgical techniques for cardiac and gastrointestinal

malformations; (ii) earlier and more effective medical treatment of infections and (iii) changed attitude both by parents, but also by medical and nursing staff in the hospitals, with a much more positive attitude towards children born with Down's syndrome (this is due to the role of non-government organizations).

The ***societal conditions*** for the lives of people with intellectual disabilities have varied dramatically. At the end of the 1980s in the countries of Central and Eastern Europe (CEE), people with intellectual disabilities lived on the edge of the society. Most frequently, these people lived in large institutions from birth to death, usually in very remote places which were surrounded by walls and that were hardly accessible for family members. Other people who where not directly involved with this problem were told and persuaded that the problem of people with intellectual disabilities had been eliminated by the high quality of health care and institutional care. This belief was supported by the fact that the streets were full of only healthy and work-eligible peoples. This misinformation served to protect some people – it protected healthy people from having to see other people suffer, it protected those with intellectual disabilities from the perceived dangers of the outside world, and finally it protected parents from the difficult care of their children.

In the Czech Republic before 1989, the placement of children born with intellectual disabilities into institutions was supported. If parents chose family care instead, they would not be supported by the state, nor often by the public at large, and hence would their lives be very difficult. Children with intellectual disabilities were not allowed to attend public education, and usually were considered "non-educable". They spent most of their time at home in the private environment, totally out of social activities. Contact with the surrounding world was only possible through their parents. Changes in the political and economical situation in CEE led also to changes in the public attitudes towards children and people with intellectual disabilities, as well as their families. Similar to the situation in other highly industrialized countries, activities in addressing the needs of person with disability are receiving encouragement and support in the Czech Republic.

Conclusion

In the Czech Republic, very low live birth prevalence rate of Down's syndrome and a low proportion of children with Down's syndrome born to women after 35-years of age support consistent detection of this type of birth defect during pregnancy and a high ratio of

terminations of pregnancies. No significant disparities in birth prevalence of Down's syndrome by maternal education in the Czech population is consistent with the fact that prenatal care is offered free and on the same qualitative level to all women. Our results show that the low occurrence of Down's syndrome in newborns is due to elective abortions, as is the case in other countries where elective abortions are legally performed.

On the other hand the higher live birth prevalence rate of Down's syndrome reflects different attitudes towards prenatal diagnosis and abortion, different social and familial background and, maybe, a much more favorable opinion towards people with intellectual disabilities.

The results suggest that birth prevalence rates of children with Down's syndrome will be in the future more and more strongly related to a range of social issues, such as the level of tolerance and "selective induced abortion behavior".

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Table 1: Medical terminations of pregnancy and birth prevalence rates of Down's syndrome according to mother's age, Czech Republic, 1994-1998

Mother´s age	Number of newborns					Pregnancy terminations		Prevalence rates of:		
	Total	Live births		Stillbirths				pregnancies with DS*	pregnancy terminat. of DS	births with DS
		Total	DS	Total	DS	Total	DS	(per 10th. births)	(per 10th. births)	(per 10th. births)
-19	46 236	46 046	17	173	0	25 606	14	6,70	3,03	3,68
20-24	202 590	201 975	87	528	0	57 992	63	7,40	3,11	4,29
25-29	143 581	143 071	71	439	0	55 454	56	8,85	3,90	4,94
30-34	60 711	60 430	42	237	2	48 606	56	16,47	9,22	7,25
35-39	19 154	19 021	20	113	0	33 644	80	52,21	41,77	10,44
40-44	3 443	3 407	9	27	0	17 321	72	235,26	209,12	26,14
45+	119	115	3	1	0	1 811	3	504,20	252,10	252,10
Total	475 834	474 065	249	1 518	2	240 434	344	12,50	7,23	5,27

Notes: * - all Dows syndrome cases (pregnancy terminations, live births and stillbirths).

Table 2: Logistic regression analysis of the birth cohort study of the differences in the birth odds* of Down's syndrome, Czech Republic, 1994-1998

	Crude	95% CI		Fully adjusted	95% CI	
	OR	Lower	Upper	OR**	Lower	Upper
Birth order						
1	1			1		
2	0,90	0,67	1,20	0,78	0,57	1,06
3+	1,82	1,33	2,48	1,13	0,76	1,68
Education of mother						
Primary	0,84	0,51	1,39	0,94	0,54	1,62
Vocational	0,88	0,58	1,34	1,11	0,71	1,74
Secondary	0,76	0,49	1,17	0,90	0,57	1,41
University	1			1		
Mother's age						
-19	1			1		
20-24	1,17	0,69	1,96	1,24	0,73	2,13
25-29	1,35	0,79	2,28	1,49	0,84	2,67
30-34	1,97	1,13	3,45	2,09	1,11	3,95
35-39	2,84	1,49	5,43	2,81	1,36	5,80
40-44	7,13	3,17	16,00	6,86	2,85	16,50
45+	70,31	20,33	243,18	65,72	18,06	239,17

Note: * - Odds of a Down syndrome birth (cases) as compared with a all births (controls);
** -Adjusted for all variables in the Table.

Table 3: Medical terminations of pregnancies (TOP) for Down syndrome and newborns with Down's syndrome according to mother's age, Czech Republic, France-Paris, and Canada, Alberta, 1998

							Live birth
Mother´s	TOP for DS		Live births with DS		Total DS*	TOP rates**	prevalence
age groups	Number	Distrib. (%)	Number	Distrib. (%)	Distrib. (%)	(in %)	rates with DS (per 10th. live births)
	CZECH REPUBLIC						
-20	4	4,1	1	1,7	3,2	80,0	1,65
20-24	14	14,3	24	40,7	24,2	36,8	6,70
25-29	20	20,4	17	28,8	23,6	54,1	5,43
30-34	22	22,4	10	16,9	20,4	68,8	7,77
35-39	22	22,4	5	8,5	17,2	81,5	12,31
40-44	15	15,3	2	3,4	10,8	88,2	28,49
45+	1	1,0	0	0,0	0,6	100,0	0,00
Total	**98**	**100,0**	**59**	**100,0**	**100,0**	**62,4**	**6,72**
-34	60	61,2	52	88,1	71,3	53,6	
35-	38	38,8	7	11,9	28,7	84,4	
	FRANCE, PARIS						
-20	0	0,0	0	0,0	0,0		0,00
20-24	0	0,0	0	0,0	0,0		0,00
25-29	8	7,8	9	25,7	12,4	47,1	9,02
30-34	31	30,4	8	22,9	28,5	79,5	7,21
35-39	36	35,3	10	28,6	33,6	78,3	15,75
40-44	27	26,5	7	20,0	24,8	79,4	44,32
45+	0	0,0	1	2,9	0,7	0,0	102,04
Total	**102**	**100,0**	**35**	**100,0**	**100,0**	**74,5**	**10,75**
-34	39	38,2	17	28,8	40,9	69,6	
35-	63	61,8	18	30,5	59,1	77,8	
	CANADA, Alberta						
-20	0	0,0	4	8,2	6,1	0,0	
20-24	0	0,0	4	8,2	6,1	0,0	
25-29	1	5,9	15	30,6	24,2	6,3	
30-34	2	11,8	8	16,3	15,2	20,0	
35-39	6	35,3	15	30,6	31,8	28,6	
40-44	7	41,2	3	6,1	15,2	70,0	
45+	1	5,9	0	0,0	1,5	100,0	
Total	**17**	**100,0**	**49**	**100,0**	**100,0**	**25,8**	**13,72**
-34	3	17,6	31	52,5	51,5	8,8	
35-	14	82,4	18	30,5	48,5	43,8	

Source: International Clearinghouse for Birth Defects Monitoring System, Annual Report, 2000
Note:
* - Medical termination of pregnancy for DS and live births with DS distribution according to mother's age groups;
** - Medical termination of pregnancy for DS per 100 cases of DS (live births and TOP) according to mother's age.

Table 4: Distribution of use of techniques of prenatal diagnosis for Down syndrome according to mother's age, Czech Republic, France-Paris, and Canada, Alberta, 1998

Technique of prenatal diagnosis Mother's age	Czech Republic	France, Paris	Canada, Alberta
Chorion villus sampling			
-35	1,02	0,98	0,00
35-39	0,00	1,96	0,00
39+	1,02	0,98	5,88
Total	**2,04**	**3,92**	**5,88**
Amniocentesis			
-35	58,16	37,25	17,65
35-39	20,41	31,37	29,41
39+	14,29	24,51	35,29
Total	**92,86**	**93,14**	**82,35**
Cordocentesis			
-35	2,04	0,00	0,00
35-39	2,04	0,98	0,00
39+	1,02	0,98	0,00
Total	**5,10**	**1,96**	**0,00**
Unknown			
-35	0,00	0,00	0,00
35-39	0,00	0,98	5,88
39+	0,00	0,00	5,88
Total	**0,00**	**0,98**	**11,76**
Total	**100,00**	**100,00**	**100,00**

Source: International Clearinghouse for Birth Defects Monitoring System, Annual Report, 2000