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EPIDEMIOLOGICAL CHARACTERISTICS OF CHILDREN BORN WITH DOWN SYNDROME IN WESTERN HERZEGOVINA IN THE PERIOD OF THE LAST TWENTY YEARS (1994-2013)

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SUMMARY

Background: *Children with Down syndrome (DS) are an everyday casuistry of pediatric clinical medicine.*

The prevalence of DS is dependent on socio-demographic and cultural conditions of a community. Antenatal screening is not carried out mainly due to religious views, and the prevalence of DS in our region is really considered a "natural phenomenon".

The aim of the study was to analyze some epidemiological characteristics of infants with Down syndrome in the western region of Herzegovina in the period between year 1994-2013.

Subjects and methods*: We performed a retrospective analysis of hospital records of children who were supervised and treated at Children's Hospital through the twenty-year period.*

Results*: In this period there were 44,100 liveborn infants. Down syndrome was detected in 78 children (54 male and 24 female). The prevalence is estimated at 1.8/1,000 of live births. Aborted fetuses and stillbirths were not analyzed. 37 (47%) of the parent couples were over 35 years of age. Out of that 65 cytogenetic analysis, a regular type of trisomy 21 was found in 94% of cases, and the translocation in 6%. From major malformations (MM) heart failure was more often present (47%), then the anomaly of the gastrointestinal and genitourinary systems. Ten children (12%) died, most often in the early period of infancy due to complications of the cardiovascular system.*

Conclusion: *The prevalence of DS throughout these two decades has been uniform in the region of western Herzegovina. Improvement in perinatal care in recent years caused higher survival and a better quality of life for the children with DS and thus their families. DS is less a desirable family tragedy, and increasingly a tolerable family fate.*

Key words: *Down syndrome - major malformations – epidemiology – prevalence - religiuos attitude*

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INTRODUCTION

It has been over 170 years since DS as a syndrome was recognized in the works of an artist, and about 150 years since it was first recorded in medical documents. The long period of research has revealed the secret of chromosomal formula on phenotype image. Prenatal testing (ultrasound of the fetus, biochemical tests and cytogenetics) allow accurate diagnosis before birth (Zergollern 1998).

The prevalence of Down syndrome is generally uniform throughout the decades of research of this phenomenon. The first national statistical reports on the prevalence in the sixties (Stevenson 1966) describe the prevalence of 1-2/1000 births as the overall prevalence of DS.

European registry for monitoring on birth defects (EUROCAT) enabled accurate recording and surveillance of birth defects in a large part of Europe (Eurocat 1990). This supervision found an interesting phenomenon regarding the prevalence of DS: Between 1920 and the early 80s of last century, the prevalence of DS decreased in many western European populations, mainly due to decreased fertility, especially in older women. The effect of prenatal screening and consequent termination of such pregnancies is also a factor. In the late eighties the prevalence of DS gently and persistently grew.

This growth is explained as a consequence of the steady increase of fertility in women in older age groups. And that growth has actually reversed the effect of prenatal screening which is still the practiced in developed regions (Olsen 2003).

In our country after the devastating war (1992-1994.) we used to monitor the prevalence of malformations per recommendations of Eurocat (Šumanović-Glamuzina 2003).

DS is the most common chromosomal abnormalities. There is the possibility of prenatal diagnosis (ultrasound of the fetus, biochemical testing) in the University Hospital Mostar and cytogenetics of amniotic fluid in some laboratories in Croatia.

But, the offered tests are rarely used by parents because of ingrained religious attitudes, which is actually the natural right of parents. Technological advances in cardio surgery and pediatric surgery, psychological and defectological monitoring of children with DS have opened a new era in medical care for persons with DS (Hayes 1997). This means that medical advances have changed the psychological attitude towards children with DS than the former attitude towards DS as a "family tragedy" to "acceptable fate of the family", at least where our environment is concerned (Miller 2013).

SUBJECTS AND METHODS

We conducted a retrospective analysis of medical records of children treated and supervised in University Hospital Mostar. The children analyzed were born in the region of Western Herzegovina between 1994.-2013. The estimated population in 2010. was about 101,000 inhabitants in this region. The analysis of all births in the hospital of Mostar, Ljubuski, Posusje, Tomislavgrad and Livno, in this period amounts to 44,000. Due to technical difficulties aborted fetuses or stillbirths were not analyzed. All live born infants with suspected Down syndrome usually were treated and monitored in University Hospital Mostar at Children's Hospital. 78 children with suspected DS were registered.

All children with suspected DS after birth were examined in detail for the presence of minor and major malformations and ultrasound analysis of the heart, brain, abdomen were performed. Cytogenetic analysis was performed in cytogenetic laboratories in Split University Hospital and University Medical Center in Sarajevo. Children are continually monitored by a physiatrist, rehabilitation specialists, speech therapists and psychologists.

This is a descriptive analysis of some epidemiological characteristics of children with DS in clearly defined geographical region.

RESULTS

From the 1994. to 2013. in University Hospital Mostar 78 children with suspected DS were registered. This gives a prevalence of 1.8/1000 newborns. Individual annual incidence of children with DS is shown in Figure 1. One exception to the common occurrence of 1-4 cases per year is the appearance of eight extra cases in the 1996. and in 2010. and seven in 2013.

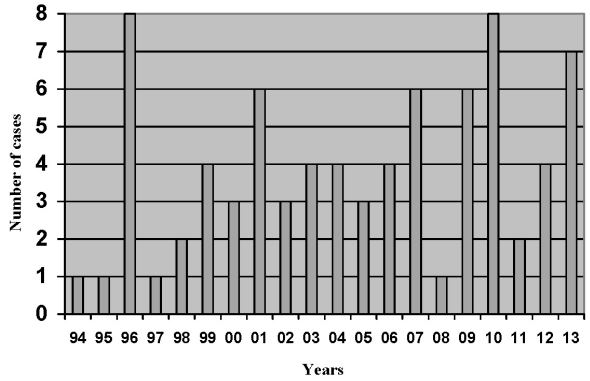

Figure 1. Down syndrome in the region of western Herzegovina in the period of 20 years (1994-2013)

Of the 78 children with DS, 54 were boys and 24 girls with a ratio of equality f/m (male/female)=2.25/1. 37 parent couples were over the age of 35 years (47%). The average age of mothers was 33 years (21-44) and of fathers 39 (25-58). The average birth weight was 3100 grams (1700-4500g). Most of the children were between the 37-41 gestational week -88.5%. Cytogenetic analysis was performed in 65 of the children (83.3%).

In 61 cases (94%) it was a regular type of trisomy 21, and in 4 cases (6%) it was a form of translocation DS. In three cases of translocation type of DS the child had extra chromosomes inherited from the mother carriers of balanced translocations (Robertson), and in one case the father was a Roberston translocation carrier. The largest number of cases of children with DS was noted in the case of parents on their second pregnancy (18/78). Fifteen pregnancies with DS were the third in a row. There was also a case of a child with DS from the twelfth pregnancy (Figure 2).

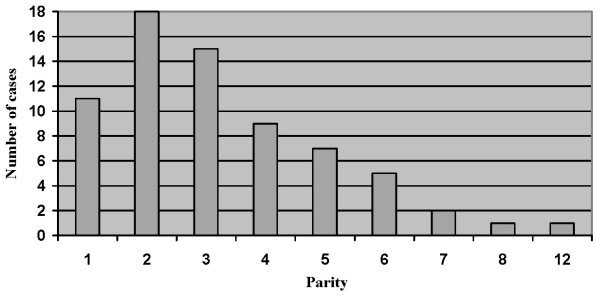

Figure 2. Parity in mothers of children with Down syndrome in the region of western Herzegovina

40% of pregnancies with DS was complicated in the prenatal and perinatal period (Table 1), The Mothers had in about 8% of such pregnancies bleeding in early pregnancy and gestosis, and polyhydramnios and psychological disturbances in about 4%. Such infants in 10% of cases had significant asphyxia at birth.

Table 1. Pregnancy and obstetric anamnesis in mothers of children with Down syndrome

Anamnesis	Number of cases	%
Normal pregnancy	48	61.0%
Bleeding in pregnancy	6	7.6%
Hypertension	6	7.6%
Asphyxia	10	12.8%
Polihydramnion	4	5.1%
Psychical problems	4	5.1%
Other	8	10.9%

Table 2. The most frequent minor malformations in children with Down syndrome in the region of western Hercegovina

Minor malformation	Number of children	%
Upward slanted eyes	56	71.7%
Malformed ears	33	42.3%
Four finger crease (simian)	38	48.7%
Hypertelorism	27	34.6%
Tonge protrusion	24	30.7%
Hypotonia	65	83.3%

Table 3. Additional major malformations in children with Down syndrome in the region of western Herzegovina

Malformation	Cardiovascular system	Gastrointestinal system	Urogenital system	Hypotyroidism
Female	16	3	3	7
Male	21	4	5	11
Total	37 (47.4%)	7 (8.9%)	8 (10.2%)	18 (23%)

The characteristic minor malformations (mM) for the DS were recorded in various combinations, usually five or more per carrier. The most frequently observed minor malformations were mongoloid slant eyes (in 72% of children). Other mM are shown in Table 2. 65 children with DS (83%) had hypotonia.

Major malformations (MM) were found in 52 children (67%). Most often cardiovascular malforamations (CVS) were present - (47%). In 8 children (10%) malformations of the urogenital system were found. In 18 cases there was a mild form of congenital hypothyroidism (23%) (Table 3). Sometimes MM of many organs were present in different combinations in one child, i.e.as multiple malformation's syndrome.

From MM of CVS most frequently was ASD I and II (Atrial septal defect primum et secundum) (63%), the AV (atrial-ventricular) channel was found in 12/78 (23%) of them. One child with DS had Tetralogy Fallot. From MM of the gastrointestinal system, five had varying degrees of obstruction of the gastrointestinal tract, one child had Mb Hirschprung, one child had an annular pancreas. From MM of genitourinary tract, 4 children had VUR (Vesico-ureteral reflux), three child had hydronephrosis and there was one child with kidney ectopy.

Neonatal complications occurred in as many as 50 children with DS (64%). It was a different level of hypoxic-ischemic encephalopathy or intracranial hemorrhage (17%) (Table 4).

Table 4. Neonatal complications in children with Down syndrome

Complication	Number of cases	%
Sepsis/Meningitis	7	8.9%
Hyaline membrane disease	2	2.5%
Perinatal infection	3	3.8%
Hyperbilirubinaemia	7	8.9%
Sy Hyperviscosum	2	2.5%
Hypoxic-ischemic encephalopathy	13	16.7%
Additional cardiological treatment	8	10.2%
Urgent surgical treatmen	8	10.2%

Eight children required additional cardio surgical treatment in specialized centers. Eight children had emergency surgical treatment (due to anomalies of the digestive tract).

Ten children (12%) died, in the early neonatal and infant period most often due to complications caused from severe congenital heart disease.

DISCUSSION

Down syndrome throughout the past two decades, is the most common chromosomal abnormalities in hospital issues the Children's Hospital in Mostar. Mostar is the regional center of the health care for all sick children of West Herzegovina and Herceg-Bosnia Canton and this region is traditionally called western Herzegovina. It is interesting to follow the prevalence of one morbidity entity over many decades in a well-defined region because it is manifested in numerous medical, social-economic and cultural phenomena.

The prevalence of DS, due to economic and cultural impacts in some countries of the world has been uniform for decades (Sherman 2007). In some countries where prenatal screening with the freedom of termination of affected fetuses is well established in everyday life, the prevalence of DS is mostly reduced to a small number, such as in Australia and Taiwan (Collins 2008, Jou 2005). However, due to delayed pregnancy and older parenthood in some developed countries (Japan, the Netherlands) in recent years, an increased prevalence of DS is recorded (Takeuchi 2008, Weijerman 2008). In large and uneven socioeconomic environments (USA), the prevalence of DS varies depending on certain social and cultural variables such as ethnicity and maternal education (Khoshnood 2003)

In our region, the prevalence over two decades is fairly uniform, with an average of 3-4 new cases in a year. The slightly higher incidence of new cases in some years (Figure 1) is a consequence of older parent couples. The prevalence of 1.8 / 1,000 is higher than in most western European countries (Loane et al. 2013), and is very similar to the prevalence in countries with similar cultural and religious background, such as in Ireland (O'Nuallain 2007).

With regard to the prenatal diagnosis of DS in our region prenatal testing (biochemical tests, ultrasound, fetal amniocentesis) are also possible but are rarely used. In the case of the recognized syndromes, mothers are choosing to deliver their child, regardless of diagnosis. Advances in Cardiac Surgery and Pediatric Surgery, supervision and monitoring of children with DS have changed the parents perceptions that the possibility of having a child with DS is an "acceptable fate" rather than a "family tragedy".

Most cases of DS in this study were children from the second, third and fourth pregnancies (54%). 30/37 parental couples of these pregnancies were over 35 years of age. We registered a child from the twelfth pregnancy. Parents were older than 35 g. High parity and occurrence of DS, is also recorded in a series of similar epidemiological studies (Doria-Rose 2003, Gusmao 2003).

Out of the 78 children with DS, the ratio of boys and girls was 2.25/1, which is similar to some studies in India and Russia (Keva 2004, Kovaleva 2001), while other analyses found more females affected with DS, such as in Chile and Kuwajt (Verma 1987, al-Awadi 1990). Cytogenetic analysis of the cases were found regular type of trisomy in 94%, and the translocation type in 6% of cases. Results were similar to those in the literature (Jones 1997).

In three cases it was a D/G and G/G translocations where mothers were carriers of balanced translocations, and on their male children were transferred unbalanced gamete. In one case it was the father as the holder of balanced translocation D/G, which is transmitted unbalanced gamete to his daughter. In all cases there were a first pregnancies. Parental pair with G/G translocation was younger than 35 years, and all parental couples with D/G translocation were aged 30-35 years. The couple with the G/G translocation had no more offspring, while other mothers delivered other healthy children and used prenatal diagnosis.

The average birth weight and gestational age are slightly higher than those from the literature (Zergollern 1998). Clearly recognizable phenotype of DS allows very rapid diagnosis almost in a hundred percent in underdeveloped areas. The most common dismorfic characteristics (called minor malformations) are shown in Tabel 2 and do not differ significantly from those in the literature (Jones 1997). Mongoloid slant eyes of children with DS were the most frequent minor stigma (72%) in our population. Hypotonia was almost always present (83%) but in varying degrees, similar to analyses of other authors (Jones 1997). In our region the recognition and documentation of the present minor stigmata was an almost sure way to the diagnosis the DS, unlike some regions where the phenotypic identification is more difficult, such as the African or Oriental populations (Christianson 1996).

The presence of major malformations in our children with DS is similar to other areas (Merrick 2001). The Most common were cardiovascular anomalies (47%), followed by genitourinary anomalies and gastrointestinal tract anomalies. Major malformations have most impact on quality of life in children with DS (Jones 1997).

Most of the pregnancies and births of the mothers were normal (60%). But, 40% of those had endangered pregnancy and childbirth and a variety of "prenatal alarm signs" that could have pointed to the present pathology (Frid 2004).

64% of the children with DS in the neonatal period had clinical complications which were vitally threatening. The most common was the presence of hypoxic-ischemic encephalopathy. Eight children required additional emergency cardiac treatment, and eight emergency surgery.

Our experience tells us that children with suspected DS should be hospitalized in the neonatology department for diagnostic evaluation. In our group, 10 children died (12%), six in the early neonatal period due to sepsis and severe cardiovascular anomalies, and the rest later in infancy.

Although children with DS require help and support from medical professionals, social services and the whole society, our experience with parents and children with DS is positive, and the advances in medicine opens new horizons in the treatment and access to it by the children and their families.

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Conflict of interest : None to declare.

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