Newborn screening for cystic fibrosis in Sicily (Italy): more benefits than harms

G. Vieni1,2, P. Fardo3, M. Lombardo2, L. Termini3, M.C. Lucanto2, G. Traverso3, M. Collura4, M.L. Furnari3, S. Faraci2, G. Magazza2, 4Ph.D. Fellowship in Clinical and biomolecular Hepato-Gastroenterology of pediatric and adult age, University Hospital “G. Martino”, Messina, Italy; 2Pediatric Department – Cystic Fibrosis and Pediatrie Gastroenterology Unit, University Hospital “G. Martino”, Messina, Italy; 3Pediatric Department – Cystic Fibrosis Regional Center, Children’s Hospital “Di Cristina”, Palermo, Italy

Objective: to evaluate the benefits of early diagnosis of cystic fibrosis (CF) through newborn screening (NS) in Sicily.

Study design: In our observational study we compared 95 screened (S) patients with 105 patients diagnosed by symptoms and/or familiarity (non-S patients), followed in the CF Centers of Messina and Palermo, both for the risk of acquisition of Pseudomonas aeruginosa, and for nutritional status during the first 7 years of life.

Results: The S patients have a significantly lower risk of chronic colonization with Pseudomonas aeruginosa during the first 7 years of life than the non-S patients. They also have a lower risk of transient/intermittent infection from the 2nd year of life, which becomes significantly lower at the age of 5, 6 and 7 years. The S patients have significantly better weight and height z-scores than non-S patients at 5, 6 and 7 years of age, and better %p/h and BMI. Patients homozygous for F508del have earlier CF manifestation and different first symptoms compared to patients with alternative genetic background of CF. Also between genotype and phenotype were many times reported. We tested whether benefits observed in our study were different from the one previously reported in CF Polish patients, diagnosed in postnatal procedure. We reported higher percentage of F508del allele (70.30 vs 56%), identified rare CFTR mutations previously not reported in Polish CF patients and completely new variants. Results of this program allowed us to estimate provisionally frequency of CF in NBS in Poland (1/5119) and carrier frequency (1/36) and in the future help us to establish the CF epidemiology and heterogeneity of CFTR mutations in Poland. Supported by: Polish Ministry of Health.

Cystic Fibrosis incidence in Lombardy over a seven year period

Y. Paracchini1, M. Seia2, L. Porcaro1, L. Costantino1, P. Capasso1, D. Degiorgetto1, D. Coviello1, C. Colombo3, T. Mariani4, C. Corbetta4, 1,2Medical Genetics Laboratory, Fondazione IRCCS Policlinico, Milan, Italy; 1Division of Epidemiology and Biostatistics, European Institute of Oncology, Milan, Italy; 3Cystic Fibrosis Centre, Fondazione IRCCS Policlinico, Milan, Italy; 4Newborn screening laboratory, A.O. Buzzi, Milan, Italy

Newborn screening for CF has been available in Lombardy (Italy) since 1983 based on IRT/IRT strategy; in 1993 F508del analysis was included in the protocol, and from 1998 the screening procedure combines IRT/IRT measurement and DNA analysis of the most common CFTR mutations. Recently, some studies reported a decreasing trend in the birth incidence of CF, possibly justified by different factors such as accessibility of a prenatal diagnosis, reproductive behaviours and population mixing.

Aim of this work was to determine the incidence of CF in Lombardy, a region located in the north western part of Italy, nearby to the Veneto area were a decrease of incidence has been observed.

The analysis was restricted to the period 2000 to 2007. We calculated the birth incidence rate of CF in each year and in the overall study period, with corresponding 95% confidence intervals (CI). We then assessed time trends in the incidence of CF by Poisson regression, and calculated the average annual percent change (AAPC) with its 95% CI. P-values <0.05 were considered significant. On average, there were about 90,000 births per year. Among the 717,172 newborns screened for CF within the study period, 157 were found to have CF. The corresponding CF birth incidence rate was 2.10 per 10,000 newborns (95%CI: 1.87–2.56). No significant time trend was observed in CF incidence in Lombardy over the study period (AAPC: −2.71%; 95%CI: −9.14% to +4.16%; p-value: 0.43).

In conclusion, CF birth prevalence appears to be stable in Lombardy.

Patients homozygous for F508del are not different at the beginning

L. Homola1,2, A. Holšíková1,2, M. Kyl1,2, I. Vášárová1, 1Faculty Hospital, Brno, Czech Republic; 2Masaryk University, Brno, Czech Republic

Background: CFTR F508del is considered to be severe mutation. Relations between genotype and phenotype were many times reported. We tested whether patients homozygous for F508del have earlier CF manifestation and different first symptoms compared to patients with alternative genetic background of CF. Also the improvement of diagnostics was examined.

Methods: Data were obtained from 52 patients (Southern Moravia CF centre, from 1977 till 2008). Patients were divided into two groups: group of homozygotes F508del with 26 subjects and group of other CFTR mutations with 26 subjects. Data collected: year of birth, very first symptom typical for CF mentioned in personal history, very first appearance of this symptom, time from CF manifestation to the final diagnosis.

Results: No statistical difference was found among two groups for time of manifestation and initial symptoms. Group of other mutations has greater variability of time of manifestation due to mild mutations included. Most common time of first CF symptom appearance is from 1 month to 16–20 months of age for both groups. Typical first symptom is malnutrition and rare fatty stools (49%), followed by respiratory tract symptoms (34%), other symptoms are in minority (18%). Diagnostics of CF in Southern Moravia has improved. During last 20 years patients from manifestation to final diagnosis significantly decreased.

Genetic aspect of two-year experience in cystic fibrosis newborn screening program in Poland

A. Norek1, A. Sobczyńska-Tomaszewska1, M. Oltarzewski1, K. Wertheim1, K. Czerwińska1, D. Sands1, K. Zybert1, J. Bat1, 1Institute of Mother and Child, Warsaw, Poland

Diagnosis of cystic fibrosis (CF) based on symptom presentation may give unreliable data about CF prevalence cause some patients may still have to be detected. CF newborn screening (NBS) provide CF infants an early intervention and opportunity to receive specialized medical care which reduce hospitalization and improves survivals. CF NBS was introduced in Poland in September 2006. The program currently covers 62% of Polish population. The screening protocol consists of IRT analysis in two blood spots, followed by DNA testing and sweat chloride test in case of IRT positive results. Molecular analysis, based on sequencing of 5 CFTR exons (7, 10, 11, 13, 21), PCR (dele2.3) and PCR-RFLP (3849+10kbC>T) analysis, allows identification of 15 most frequent mutations in Polish population and about 370 rare variants. Since September 2006 till the end of October 2008, 419 783 newborns were screened by IRT. Of those, 2953 were screened for CFTR mutations. 264 infants were positive; 61 had mutations in 2 alleles of CFTR gene and 59 of them were confirmed as having clinical symptoms of CF disease, 203 had mutation in 1 allele with 7 of them presented clinical CF symptoms. The spectrum of CFTR variants was significantly different from the one previously reported in CF Polish patients, diagnosed in postnatal procedure. We reported higher percentage of F508del allele (70.30 vs 56%), identified 8 rare CFTR mutations previously not reported in Polish CF patients and completely new variants. Results of this program allowed us to estimate provisionally frequency of CF in NBS in Poland (1/5119) and carrier frequency (1/36) and in the future help us to establish the CF epidemiology and heterogeneity of CFTR mutations in Poland. Supported by: Polish Ministry of Health.