224 Genotype–phenotype correlation of pancreatic function in children with cystic fibrosis

S. Sciuca[1], O. Turcu[1], G. Posselt[2], B. Tümmler[3]. [1]*State Medical and Pharmaceutical University, Pediatrics, Chisinau, Moldova;* [2]*University Hospital of Johann Wolfgang Goethe, Pediatrics, Frankfurt/Main, Germany;* [3]*Medical University of Hannover, Hannover, Germany*

Objective: To assess the level of fecal elastase-1 (FE-1) in relation to CFTR gene mutations in patients with cystic fibrosis (CF).
Materials and Methods: This study included 49 patients (23 boys) with CF, mean age 8.43±0.99 years. CF was established on the basis of a positive sweat test (Macroduct, Wescor USA) and the results of molecular genetic analysis. Genetic diagnosis was realized for 36 CFTR mutations in genetic laboratories from Germany and France. To detect pancreatic insufficiency (PI) was defined FE-1 (ScheBo Biotech, Germany). The values of FE-1 in the range 0–100 μg/g, are characteristic for severe exocrine PI, 100–200 μg/g for moderate exocrine PI, and >200 μg/g for pancreatic sufficiency.
Results: F508del mutation was revealed in 73.33% cases (40.0% – homozygotes), known genotype with other mutations was found in 18.26% cases. Low values of FE-1 (7.89±3.70 μg/g) confirmed exocrine PI in 81.64% patients with CF. PI with FE-1 of 2.90±0.78 μg/g was confirmed in 100% children with homozygous state of F508del mutation. F508del mutation in heterozygous state caused decreased levels of FE-1 (33.69±19.34 μg/g). Only 5.88% patients with CF F508del heterozygous were pancreatic sufficient and other 11.7% cases were moderate PI. Non-F508del CFTR mutations determined FE-1 levels of 218.64±64.87 μg/g, with PI in 57.89% patients.
Conclusion: The F508del mutations in homozygous state were associated with severe pancreatic exocrine insufficiency in all patients. Heterozygous state of mutation F508del requires association with another mutation and in most cases led to pancreatic enzyme deficiency. Non-F508del CFTR mutations are not obligatory associated with PI.

225 PIP score could predict the risk of pancreatitis in patients with cystic fibrosis (CF)?

S. De Santis[1], A. Casale[1], N. Amato[1], V. Terlizzi[1], F. De Gregorio[1], A. Tosco[1], A. Sepe[1], V. Raia[1]. [1]*University of Naples 'Federico II', Pediatrics, Naples, Italy*

Objectives: Pancreatic insufficiency (PI) occurs in typical CF phenotype when patients carry two severe mutations on both alleles. When at least one mutation is mild, pancreatic function is preserved and pancreatitis can occur. Our aim is to confirm in small number of CF patients whether the risk of pancreatitis could be predicted by PIP (pancreatic insufficiency prevalence) score, according to the Canadian Consortium for CF Genetic Studies (CCCFGS).
Methods: We examined 164 CF patients [113 PI and 51 pancreatic sufficient (PS)] with identified mutations on both alleles from the CF Regional Centre of Naples. 9/164 patients showed at least one episode of pancreatitis (PANC). We classified their mutations in severe and mild according to CF Mutation Database (www.genet.sickkids.on.ca). PIP score was calculated as PI/ PI+PS patients carrying the same mutation when in homozygous or in heterozygous with a severe one. We applied the PIP score on each CF patient to determine their risk of pancreatitis, using the lowest PIP score among the two identified mutations. According to the cut-off defined by CCCFGS, we divided CF genotype of our patients into mild (PIP $\leqslant$ 0.25) and severe-moderate (PIP > 0.25). Patients with PANC and without PANC showed a PIP score $\leqslant$0.25 5/9 (56%) and 36/155 (23%) respectively.
Conclusions: The percentage of patients with PIP score $\leqslant$0.25 was higher in patients with PANC rather than in patients without PANC; the difference between the two groups was statistically significant ($p < 0.05$). As CFTR genotype seems to be pivotal in the development of pancreatitis, the PIP score could be a prognostic tool concerning the risk of pancreatitis, as previously suggested.

226 Intestinal inflammation in CF: stool markers and correlation with pancreatic enzymes

C.Y. Ooi[1,2], J.M. Lee[1], S. Leach[1], T. Katz[2], A.S. Day[3], A. Jaffe[1,2]. [1]*University of New South Wales, School of Women's and Children's Health, Faculty of Medicine, Sydney, Australia;* [2]*Sydney Children's Hospital Randwick, Randwick, Australia;* [3]*University of Otago, Paediatrics, Christchurch, New Zealand*

Intestinal inflammation is present, in varying degrees, in cystic fibrosis (CF). The cause of inflammation is unclear but likely multi-factorial. The primary aim was to define the stool calprotectin and S100A12 levels as markers for intestinal inflammation in CF. The secondary aim was to define the relationship between intestinal inflammation and pancreatic enzyme therapy (PERT).
Methods: Stools were collected in children with CF for calprotectin and S100A12 measurement. Comparisons were made to levels in healthy children (HC) and children with active inflammatory bowel disease (IBD). Pancreatic function status (sufficient [PS] or insufficient [PI]) and PERT dose were determined.
Results: 39 CF patients (median [range] yrs: 3.5 [4–18]), 31 IBD patients (3.3 yrs [2.4–16]) and 30 HC (3.6 yrs [2.2–15.5]) were recruited. CF patients had significantly higher stool calprotectin levels compared with HC (median = 71.9 *vs.* 30.5 mg/kg; $p = 0.005$), but lower than in IBD (median = 1265 mg/kg; $p < 0.0001$). Higher stool calprotectin levels were seen in those with PI (n = 35) than in those with PS (n = 4) (median = 92.2 *vs.* 30.8 mg/kg; $p = 0.037$). There was no significant difference in stool S100A12 levels between CF and HC (median = 0.4 *vs.* 1.2 mg/kg; $p > 0.05$) but stool S100A12 was significantly raised in IBD (median = 55.2 mg/kg; $p < 0.05$) compared to both CF and HC. There was no correlation between stool calprotectin levels and PERT dose (r = –0.08; $p = 0.6$).
Conclusion: Stool calprotectin but not S100A12 levels were raised in CF, especially PI patients. There was no association between PERT dose and intestinal inflammation. These data may provide insight into the intestinal inflammatory pathways involved in CF.

227 Plasma citrulline levels in cystic fibrosis patients

H.P. Ioannou[1], M. Fotoulaki[2], P. Augoustides-Savvopoulou[1]. [1]*Hippokration Hospital, 1st Pediatric Department of Aristotle University, Thessaloniki, Greece;* [2]*Papageorgiou General Hospital, 4th Pediatric Department of Aristotle University, Thessaloniki, Greece*

Background and Objective: The small intestine is one of the main sites of cystic fibrosis (CF) manifestations and non-pancreatic intestinal factors are suggested to contribute to fat malabsorption. Recent findings suggest that the small bowel mucosa of CF patients frequently demonstrates inflammatory changes. Citrulline is a non-protein amino acid synthesized in the small intestine and its plasma levels have been proposed as a reliable intestinal marker in various conditions. The objective of the present study was to investigate the value of plasma citrulline levels as a marker of intestinal inflammation in cystic fibrosis (CF) patients.
Methods: Thirty-six stable CF patients (age range 13 to 28 years) without overt gastrointestinal symptoms and 36 age-matched controls were included in the study. Plasma citrulline levels were measured by ion-exchange high performance liquid chromatography. Possible relationship of plasma citrulline levels to the nutritional status of CF patients was also studied.
Results: Plasma citrulline levels did not statistically differ between CF patients and age-matched controls (38±7 μmol/L and 39±11 μmol/L respectively). Nine patients were malnourished while 27 patients had normal nutrition. Comparison of plasma citrulline levels between patients with malnutrition and patients with normal nutrition did not reveal any differences, either (37±7 and 38±8 μmol/L respectively).
Conclusions: Plasma citrulline did not appear to be a sensitive marker of intestinal inflammation in stable CF patients. The presence of malnutrition did not affect plasma citrulline levels and our results agree with previous reports in conditions other than cystic fibrosis.