Cystic Fibrosis is an autosomal recessive disease that is caused by over one thousand mutations at the cystic fibrosis conductance regulator gene (CFTR). The aim of this study was to determine the frequency of the most frequent mutation in this disease, called F508del, in Venezuelan patients with CF using Polymerase Chain Reaction (PCR) and automated sequencing. We studied a first group of 122 patients who are included in the national program of CF, which have symptoms compatible with CF, without considering their provenance. The second group of 28 patients consisted in selected Venezuelans who were third generation and who had at least two electrolyte determination tests above 60 mEq/L. Detection of the mutation was performed by PCR amplification of a 500 (pb) CF gene segment which contains the 508 protein position and automated sequencing at ABI3130XL. In the first group the F508del allele frequency was 27% vs. 73% WT allele, distributed in 22 homozygous and 26 compound heterozygote F508del/X, in the second group the F508del allele frequency was 23% vs. 77% WT allele, distributed in 3 homozygous and 7 compound heterozygote F508del/WT, which suggests no significant (p>0.05) influence of the provenance of the patients. Our results are in agreement with previous reports that shows a F508del frequency highly heterogeneous in Latin-American countries. This variation can result from mixed populations with a different genetic background and new mutations in CFTR. The result also indicates a high percentage of mutations causing FQ different to 508, which should be included by other exons in the diagnosis of this disease in the studied population.

Cystic fibrosis transmembrane regulator gene mutations (CFTR) in a tertiary care centre in Saudi Arabia

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Objective: To determine the Cystic fibrosis trans-membrane regulator gene (CFTR) mutations in Saudi Arabia (KSA).

Study design: Retrospective chart review of all diagnosed CF patients and determine their CFTR mutations during the period 2000–2011.

Results: A total of 317 patients were confirmed to have CF with typical clinical picture and sweat chloride test >60 mmol/L. A total of 272 patients had their CFTR examined, but only 241 (89%) patients have identified CFTR mutations. A total of 30 mutations were identified. Thirteen new mutations that have never been described before in the medical literature were identified. Two hundred and ten patients (91%) were homozygous and 20 (9%) patients were compound heterozygous. Eleven patients their DNA could not be identified with the present testing. Of the most common mutations that have been identified in descending frequency were: 1548delG in 49 alleles (20.5%), DF–508 in 36 (15%), I1234Vin 27 (11.5%), 3120+1G→A in 27 (11.5%), 711+1G→A in 24 (10.5%), and H139L in 20 (8.5%), which identified 77% of our CFTR mutations. Fifteen private mutation were identified in 15 different families.

Conclusion: CFTR mutations in Saudi Arabia differ from that described in the western world. Specific attention to the Saudi CFTR mutational patterns should be applied during screening for such disease in this part of the world.

Cystic fibrosis in Egypt: New mutational detection of the CFTR gene in patients from Alexandria, northern Egypt

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Background: The knowledge about cystic fibrosis (CF) in Egypt is very limited, and a few reports have drawn attention to the existence of CF or CFTR-related disorders in Egyptian population (Naguib et al., 2007). Furthermore, Egypt is a Mediterranean North African country in addition to its pharaonic origin, and gene flow to its population occurred from Ethiopian, Greco-Roman, Arab, Turkish, French, English settlers (Temtamy et al., 2010). Thus, the aim of this investigation was to perform molecular analysis to identify the CFTR gene mutation in patients from Alexandria (northern Egypt) to establish a list of Egyptian CFTR mutations.

Methods: DNA samples of 37 Egyptian patients were screened for the CFTR gene mutations. All 27 exons and its flanking introns of CFTR were amplified by PCR using the published primer pairs and were studied by direct sequencing to identify disease-causing mutations.

Results: As a result of this screening, only four mutations were found: c.1418delG mutation in exon11, c.2620–15C>G mutation in exon16, and c.3877G>A (p.Val1293Ile) mutation in exon 24 and a novel mutation c.3718→24G>A in intron 22. Moreover, six polymorphisms were identified: c.1408A>G (M470V), c.3870A>G (P1290P), c.2562T>G, c.1584G>A, c.4389G>A, c.869+1C>T. All of these mutations and polymorphisms are not previously detected in the Egyptian population except for the c.1408A>G (M470V) polymorphism.

Conclusion: Our preliminary data show that detected mutations in the CFTR gene are strongly associated with CFTR-RD and only one disease-causing mutation was identified. These findings will be used for planning future screening of CFTR mutation in the Egyptian population.

Genotype–phenotype correlation of CFTR p.Leu206Trp mutation in 22 paediatric and adult cystic fibrosis (CF) patients

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Introduction: CFTR p.Leu206Trp mutation is associated with residual transmembrane transport of chloride and mild CF.

Objective: To analyze the clinical differences between paediatric and adults CF patients who are compound heterozygous for p.Leu206Trp.

Methods: We examined clinical retrospective data of 12 paediatric patients (group A: 6 males ranging 4 months to 12 y) and 10 adults (group B: 6 males, 27–51 y) harbouring p.Leu206Trp. Clinical symptoms, sweat test (ST), pulmonary function (PF), pancreatic sufficiency (PS), air trapping (AT) bronchiectasis (BC) on CT scan and colonization with Pseudomonas aeruginosa (PA) or Staphylococcus aureus (SA) were analyzed.

Results: Patients in group A were diagnosed by newborn screening (NS) and adults at mean age of 30y. 8 adults were diagnosed by respiratory symptoms and had BC on CT compared with only 5 in paediatric patients. ST values were borderline at NS period (except in one case) but become positive with increasing age. In adults, ST values were positive. All the patients except one were PS in both groups. FEV1 predicted values were normal in group A but in 60% of adults values were abnormal. PA and SA were isolated occasionally in paediatric patients but all adults were chronic colonized.

Conclusions: We found clear differences between paediatric and adults patients heterozygous for p.Leu206Trp. In childhood is associated with mild disease but patients diagnosed in adulthood have lung disease, chronic colonization with PA/SA and diffuse BC. Identification at NS of the p.Leu206Trp in patients with other identified mutation and borderline ST values could allow early treatment to delay lung disease in adulthood.