P005

Seven-year follow-up of patients with cystic fibrosis after newborn screening program

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Objectives: We aimed to examine 7 years results of newborn screening program (NBS) in Turkiye.

Methods: All children registered in the Turkish National Cystic Fibrosis Registry System in 2022 and born after 2015 -when screening first started- were included in study. Patients were divided into 3 groups according to NBS results: Group 1; NBS was positive, Group 2; NBS was negative, Group 3; never been screened and NBS results are unknown. All clinical and demographic data were compared between the 3 groups.

Results: There was a total of 931 patients, 52% of them were male. 78 patients were excluded due to missing data. There were 668 patients in Group 1, 90 in Group 2 and 95 in Group 3. The age at diagnosis was 0.17 (0.08–0.33) months in Group 1, 0.50 (0.25–1.0) months in Group 2 and 0.33 (0.17–0.75) months in Group 3, respectively ($p < 0.001$). The first sweat test was 76 mmol/L (59–86) in Group 1, 63.0 (50.25–79.5) in Group 2 and 76 (56–89.75) in Group 3 ($p = 0.02$). The second sweat test was 76 (59,75–87) in Group 1, 59.50 (42.75–78.75) in Group 2 and 65 (54–79) in Group 3 ($p = 0.006$). 101 patients could perform pulmonary function test. Median FEV1(%) was 88 (77–103) in Group 1, 90 (71.5–104) in Group 2, 89.5 (81.75–97.5) in Group 3 ($p > 0.05$). There were no differences between the group in terms of number of pulmonary exacerbations, hospitalizations and days of iv antibiotics, chronic pseudomonas colonization ($p > 0.05$). 48% of the patients had severe genotype, 18% had a mild mutation genotype and 33.2% were unknown. Severe mutation genotype was detected most frequently in Group 1 ($p = 0.021$).

Conclusion: Negative NBS result can delay CF diagnosis. Lower sweat test results in the group with negative NBS may also contribute to the delay in diagnosis. Further evaluation should be performed in patients with clinical suspicion, even if the NBS result is negative.

P006

False negative newborn screen and absent clinical features of cystic fibrosis after *in utero* modulator exposure for an infant with two cystic fibrosis causing mutations

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An infant at our center was born with cystic fibrosis (CF) but was not identified by immunoreactive trypsinogen (IRT) on the newborn screen (NBS). Because the NBS method relies on elevated IRT to determine if a sample is run for cystic fibrosis transmembrane regulator (CFTR) mutations, the NBS was "negative". A request for *CFTR* analysis revealed two CF-causing mutations: F508del and E92X. The child's mother has CF and was on highly effective modulator therapy (HEMT) throughout the pregnancy. The newborn's clinical evaluations were noted for normal hepatic labs, eye exam, urologic exam, and fecal elastase (FE-1). He had an elevated serum lipase and sweat chloride (SC) values. He was born with minimal target organ damage due to CF. The objective was to try to prevent his withdrawal from HEMT and subsequent organ damage from CF. He was unable to breastfeed and get HEMT through breast milk. He was started on a weight-based dose of elexacaftor/tezacaftor/ivacftor (E/T/I) calculated based on the maximum dose per kilogram of approved doses for ivacaftor. Predetermined clinical objectives were measured: maintaining normal FE-1, reducing pancreatitis, and normalising SC. The low starting dose was effective at reaching the goals for his pancreas but not SC. The dose was increased to half maximum E/T/I, and his sweat chloride fell below 30 mmol/L. This met the clinical goal of having his SC fall below the range that is typical for congenital absence of the vas deferens and male infertility in CF. He remains on 2.5 mg/kg of E/T/I based on the ivacaftor component until he is old enough for approved E/T/I dosing. His FE-1, lipase, and SC remain normal and his vas deferens remains palpable. Whether he will have preserved fertility cannot be determined until he passes puberty.

Age (weeks)	4	19	25	47	59	73
E/T/I + I dose (mg/kg)	0	1.25	2.5	2.5	2.5	2.5
Sweat chloride (mmol/L)	62	47	26.6	26.9	26.4	27.8

P007

Long term clinical follow up of patients with cystic fibrosis transmembrane conductance regulator-related metabolic syndrome (CRMS/CFSPID)

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The conversion of CRMS/CFSPID to CF and their long-term follow-up are a matter of curiosity all over the world.

Aim: To observe the long-term follow-up and diagnostic conversion of CRMS/CFSPID cases to CF at our tertiary care hospital.

Method: CRMS/CFSPID diagnoses and follow-up of children who were referred to our center between January 1, 2015, and December 31, 2023 due to a positivity in the newborn screening test and whose first sweat chloride test measured in our center was between 30 and 60 mmol/L were evaluated retrospectively. Since there was no mutation study in our screening protocol, patients who presented with a positive screening test and those whose sweat chloride test was <30 mmol/L could not be followed up and were therefore excluded from the study.

Results: We identified 78 infants (44 boys and 34 girls). We obtained the IRT/IRT(immune reactive tripsinojen value of 65 infants whose newborn screening was positive. In all patients, the IRT-1 median value was 109.9 (51.04–235) μg/l, and IRT-2 median value was 81.72 (35–172) μg/l. There was no correlation between IRT-1 and IRT-2 values and the first sweat chloride test levels ($p > 0.05$). Among the CRMS/CFSPIDs who are on clinical follow-up: