The use of sweat chloride test for screening cystic fibrosis among malnourished children suffering from frequent respiratory infections

To the Editor

I have 3 comments on the interesting study by Abu-Alshiekh et al[1] on the use of the sweat chloride test for screening cystic fibrosis among malnourished children suffering from frequent respiratory infections.

First, once upon a time, it was thought that cystic fibrosis (CF) is purely confined to the Western countries. However, recent epidemiological studies have demonstrated its existence in many parts of the world, including Arabian countries. The changing incidence of CF in Jordanian neonates from 1 per 2560 live births in 1992 to 39 per 100,000 live births in 2004[2] is interesting. The high consanguinity rate, particularly first cousin marriages (69%), and the large family size in Jordan has significantly contributed to the prevailing of rare and new autosomal recessive conditions, including CF.[3] Pediatricians should be thoroughly knowledgeable of CF in children. Alshiekh et al[1] did well in their attempt to define the cut-off reference value for sweat chloride in children with CF that would help pediatricians approach ambiguous or indeterminate cases of CF, as children with CF are anticipated to markedly increase in the near future.

Second, the sweat chloride test remains an important laboratory test to support the diagnosis of CF. Abu-Alshiekh et al[1] stated in their study that the sweat chloride level of >57mmol/L seems to strongly suggest the likelihood of CF in the studied Jordanian patients. This cut-off value seems questionable in the following terms: 1) It was applied to all patients with CF despite age or gender. 2) The reference values of sweat chloride in healthy Jordanian children have not yet been developed. In an Australian study,[4] it was found that sweat chloride increased with age, with the rate of increase slowing progressively to zero after the age of 19 years. The estimated medians (95% reference interval) for sweat chloride were: 5-9 years, 13 mmol/L (1-39 mmol/L); 10-14 years, 18 mmol/L (3-47 mmol/L); 15-19 years, 20 mmol/L (3-51 mmol/L); and >20 years, 23 mmol/L (5-56 mmol/L). Therefore, constructing age and gender-related reference intervals for sweat chloride in both healthy Jordanian children and those with CF is crucial as this will be of utmost usefulness to the pediatricians interpreting sweat chloride results. 3) The installed cut-off value might not be able to precisely detect 2% of atypical cases of CF.

Third, the cut-off value of sweat chloride level installed by Abu-Alshiekh et al[1] does not support the increasing concerns nowadays on the validity of the "golden rule of 60" in precisely diagnosing CF, particularly in borderline sweat chloride concentrations. In a recent Italian study,[5] the relationship between CF trans-membrane conductance regulator gene (CFTR) mutation analysis and sweat chloride concentration was investigated in a cohort of subjects with borderline sweat test values, to identify the misdiagnosis of CF. The mean value of sweat chloride concentration in the deoxyribonucleic acid (DNA) negative subjects was lower than in those with at least one CFTR mutation. The study concluded that a sweat chloride concentration of 39 mEq/L is the best sensitivity trade-off for the sweat test with respect to genotype. Moreover, the full-blown clinical picture of CF might be associated with negative sweat test and borderline sweat chloride levels. Therefore, extensive CFTR gene mutation analysis and nasal potential difference (NPD) measurement remain critical to establish the diagnosis of CF, particularly in patients with symptoms suggestive of CF and intermediate sweat chloride values (30-60 mmol/L).

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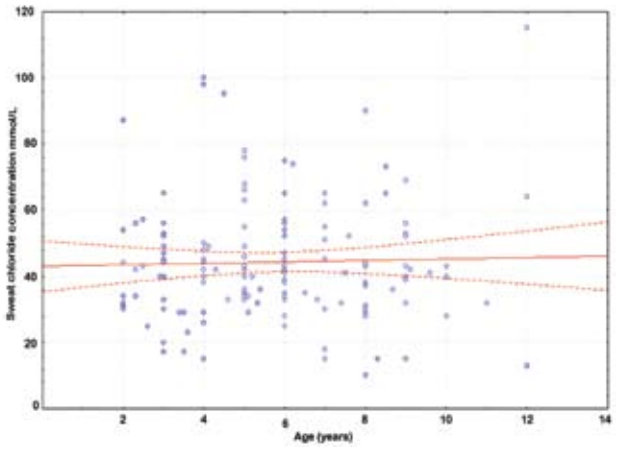
Reply from the Author

We would like to thank Prof. Al-Mendalawi for his comments on our article. As the sweat chloride concentration (mmol/L) in this study had no age-related change as shown in **Figure 1**, and in addition, there were no differences between males and females, therefore, the results obtained were not divided according to gender and age in our sample (p>0.05). Moreover, the sample was restricted to children of the age range from 2-12 years. There was a statistically significant difference in the sweat chloride concentration among both the positive polymerase chain reaction (PCR) CF group and the second negative PCR CF group, and these were favored to determine the best cut-off values for CF discrimination. Our independent study used a Receiver Operating Curve (ROC) analysis to find the best sweat chloride concentration cut-off value (>57 mmol/L) for screening CF in the North of Jordan, and was found



somewhat consistent with other studies in Jordan,[6] Egypt,[7] and France.[8] However, the results differ from other studies from Italy,[9] and Belgium,[10] which found a sweat chloride concentration cutoff value of <57 mmol/L.

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Related topics

Abu-Alshiekh NK, Kofahi SM, Nusair ZM. The use of sweat chloride test for screening cystic fibrosis among malnourished children suffering from frequent respiratory infections. ***Saudi Med J*** 2009; 30: 1526-1531.

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Abu-Alshiekh NK, Kofahi SM, Nusair ZM. The use of sweat chloride test for screening cystic fibrosis among malnourished children suffering from frequent respiratory infections. ***Saudi Med J*** 2009; 30: 1526-15231.